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IN MEMORY OF ACADEMICIAN S. I. VAVILOV

The untimely death of Academician S.I.Vavilov is a serious loss for the entire Soviet people. In him our fatherland has lost an outstanding statesman, a highly gifted scientist, and an ardent propagandist of the great ideas of communism.

S.I.Vavilov was born in Moscow in 1891. In 1909 he matriculated in the Physical-Mathematical Faculty of the University of Moscow and in his second year began experimental work in the laboratory of the brilliant Russian physicist P.N.Lebedev. The research paper written by S.I.Vavilov during his student days on "The Thermal Fading of Dyestuffs" won him the gold medal of the Society of Friends of Natural Sciences of the University of Moscow.

As one of the most highly gifted students, S.I.Vavilov was given the opportunity of doing graduate work at the university in preparation for a scientific career, but he turned down an offer of this sort. The reason for his rejection of the offer was the mass exodus of the most progressive scientists of the time from the university, including his own teacher, P.N.Lebedev, in protest against the persecution of progressive professors.

S.I.Vavilov was in military service from 1914 to 1918. He fought in World War I first as a sapper and toward the end of the war as assistant to the commander of a radio division. Sergei Ivanovich carried out important researches in radio physics under difficult front-line conditions.

After his return from the front, Vavilov concentrated wholly on scientific research and teaching. His life and career during the twenties were associated with the major scientific and educational institutions of Moscow: the University of Moscow, the Bauman College of Engineering, and the Institute of Physics and Biophysics. It was during these years that he established the fundamental laws of luminescence and proposed its practical utilization, including the manufacture of luminescent lamps, in particular. At the same time, Vavilov proved to be a talented polularizer of science.

The election of S.I.Vavilov as corresponding member of the USSR Academy of Sciences in 1931 was in recognition of his scientific achievements; he was elected to full membership in the USSR Academy of Sciences in 1932.

It was in that same year 1932 that he became head of the Physical Section of the Institute of Physics and Mathematics of the USSR Academy of Sciences at the request of V.L.Komarov, at that time vice-president of the Academy of Sciences.

It was from this time on that the role to be played by S.I.Vavilov in the organization of Soviet science became strikingly clear. Starting with a tiny physical laboratory, he set up the P.N.Lebedev Institute of Physics within the framework of the USSR Academy of Sciences, which is one of the leading scientific institutes in our country.

In June, 1945, S.I.Vavilov was elected president of the USSR Academy of

Sciences. In this high post, as an organizer of scientific research, he proved himself to be fully worthy of the great confidence placed in him by the Party and the government. He gave all of his energy to the profound and manysided development of advanced Soviet science in the Stalinist epoch, resolving the scientific problems involved in the achievement of the great task of constructing communism in our country.

Vavilov's activity during this period was astonishingly far-ranging and manysided. He was president of the USSR Academy of Sciences, president of the Committee to Coordinate the Scientific Work of the Academies of Science of the Union Republics, editor-in-chief of the Great Soviet Encyclopedia, and director of the Institute of Physics of the USSR Academy of Sciences, though this by no means exhausts the enumeration of the posts he occupied. Vavilov managed to combine an extraordinary amount of scientific organizing work with his own scientific research. During the thirties and the forties he developed the theory of the extinguishing of luminescence by foreign bodies and the theory of concentration extinguishing, and suggested new interference and polarization methods of investigating elementary radiators; together with his pupils he discovered and investigated a new form of luminescence, arising when electrons move in a medium at velocities in excess of the velocity of light; he studied the nature of the quantum fluctuations of light; and, finally, luminescent lamps were developed and manufactured under his supervision.

In a chemical journal it is appropriate to make special mention of Vavilov's contributions to chemical science. The results of Vavilov's initial researches, dealing with the photochemical and thermal fading of dyestuffs, have become part of all monographs on photochemistry. The polarization methods proposed by him for studying the anistropy of complicated organic molecules, which were extensively developed in the work of his pupils, are being successfully employed by numerous research workers. His theory of the migration of energy between molecules in solutions is of considerable importance in biology as well as in chemistry.

As far back as the twenties, Vavilov, together with V.L.Levshin, introduced the concept of the metastable state of organic molecules, which has become of such importance in chemistry in recent years. The researches of Vavilov and his pupils on the extinguishing of the fluorescence of solutions by foreign substances have made it possible to provide an answer to one of the most difficult problems in chemical kinetics: how should the number of effective collisions between reacting molecules in solutions be computed?

As a man of profound and manysided culture, S.I.Vavilov not only made a thoroughgoing study of the great doctrine of Lenin and Stalin, but employed it creatively. Some of Vavilov's most important papers deal with problems of philosophy, history, and methodology of science. An ardent patriot, Vavilov fought for the priority of his own country's science.

S.I.Vavilov won the love and respect of the toilers of our country by his supreme services to this people and to the great cause of communism. He was a deputy to the Supreme Soviet of the RSFSR and the Supreme Soviet of the USSR and a deputy of the Moscow and Leningrad City Soviets.

The Soviet government regarded the outstanding services of Academician S.I.Vavilov to his country highly. Vavilov was twice awarded the Order of Lenin and was awarded the Order of the Red Banner of Labor and medals of the Soviet Union. He was twice awarded the Stalin Prize for his scientific achievements.

B.Sveshnikov

THE RATE OF SOLUTION AND THE POTENTIAL OF DISSOLVED IRON

Ya. V. Durdin and M. A. Oranskaya

In our previous paper [1] we published the results of our investigation of the rate of solution and the potential of dissolving chromium in hydrochloric and sulfuric acids. The present research was undertaken with a view to learning how far the behavior patterns observed in the dissolution of chromium hold good for the dissolution of other metals.

Thanks to the researches of M. Tsentnershver on the rate at which cadmium, tin, and aluminum dissolve,* we were able to assert, at the time this investigation was carried out, that the representative type of relationship derived by us for the rate of solution of chromium as a function of the concentration of hydrochloric acid was qualitatively analogous to the corresponding relationship derived by Tsentnershver for the rates at which the above-mentioned metals dissolve [3].

Tsentnershver's data on the rate of solution of iron carbonyl did not enable one to estimate the variation of this rate with the acid concentration [4].

An exponential equation expressing the variation of the rate at which iron dissolves with the concentration of hydrochloric acid was derived by Conroy [5].

A. Sieverts and P. Lueg [6] made a study of the dissolution of iron wire in 4 N, 5 N, and 6 N hydrochloric acid and in 4 N and 8 N sulfuric acid and came to the conclusion that the rate at which iron dissolves in hydrochloric acid is proportional to $(C_{HCl})^3$, while in sulfuric acid the rate is proportional to somewhat less than the first power of the acid concentration.

Owing to the primitive methods employed, however, we were unable to regard the results of these investigations as any more than rough approximations. S. Ram, in his investigation of the rate at which low-carbon iron dissolves in sulfuric acid, found that the rate of solution of iron rises approximately proportionally to the acid concentration in the region of moderate concentrations of sulfuric acid. At high concentrations (ca. 16 N H_2SO_4) the rate at which the iron dissolves drops sharply, the iron becoming passive [7].

Damon, in his investigation of the dissolution of steels containing various percentages of carbon in sulfuric acid, reached a similar conclusion, [8]. Closest to our research is the investigation made by A.I. Krasilshchikov [9], who made a study of the rate at which commercial sheet iron dissolves in hydrochloric and sulfuric acids at concentrations ranging from 1 N to 10 N.** The general nature of the expression for the variation of the rate of solution of iron with the concentration of hydrochloric or sulfuric acid derived by that author is close to what we derived for chromium as well as for iron.

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*This investigation was completed before the war, part of it having been published in the Scientific Papers of Leningrad State University for 1940 [2].

**As well as in nitric acid in which the controlling factor in the kinetics of the dissolution of iron appears to be the diffusion process.

Unfortunately, in nearly all these investigations of the rate of solution of iron, the rate was determined by the gravimetric method, i.e., by the loss of weight of the metal throughout the experiment, and hence represents merely the average rate applying to the whole test. Owing to the differences in the length of the induction period at various acid concentrations, this rate may differ considerably from the iron solution rate for a stationary state. Moreover, in these researches no investigation was made of the effect of stirring the solution upon the rate at which the iron dissolves, nor (what is particularly vital for us) was the potential of the dissolving iron measured. We therefore believe that the data we obtained on the solution rate and on the potential of dissolving iron are not without interest even today.

1. Experimental method. The experimental method employed in this research was essentially similar to the method described in our previous reports on magnesium [10] and chromium [1]. We might mention that the rate at which the iron dissolved was measured in the same reaction vessel, with a capacity of 1.5 liters, in which the solution rate of chromium had been measured; we shall therefore discuss at this point merely some features that were specifically characteristic of the present research.

In this research we investigated the rate of solution and the dissolution potential of Armco iron containing the following impurities:

C 0.017% Si 0.02% Mn 0.0006% P 0.01% S -

For the sake of comparison we also investigated the rate of solution of commercial light sheet iron.

We prepared plates 1.5 x 2.0 cm in size* for these tests, the plates being affixed to a metal holder by dental cement as described in our paper on chromium. The back and the edges of the plate, as well as the dental cement, were covered with bakelite lacquer, which was polymerized as described in our paper on chromium. The front surface of the plates was cleaned with fine glass paper. It should be noted that the plates of Armco iron were about 7 mm thick. Because of this appreciable thickness, the basic series of tests using Armco iron was performed on a single plate. The plates made of light sheet iron were used up in one or two tests as a rule. Connection to the potentiometer circuit was made at the upper edge of the plate by means of a copper wire soldered to the upper edge of the iron plate, which was under a glass bell and was insulated from the acid solution by the dental cement and bakelite lacquer, the end of the wire being led out through the inner tube of the metal holder as described in our previous paper on chromium.

The solutions were prepared, as in our research on chromium, with chemically pure hydrochloric acid and sulfuric acid "pure, for analysis". All the basic tests were run at a temperature of 60 ± 0.2°. We chose so high a temperature because the rate at which Armco iron dissolved at lower temperatures was too low.

The units used in measuring the rate of solution of iron and its potential were the same in this research as in our research on chromium, i.e., the solution rate is expressed in cubic centimeters of hydrogen evolved per sq. cm. of metal surface per minute. The potential is expressed in millivolts against a saturated calomel electrode, its sign being taken as plus (+). The intensity of stirring was indicated by the stirrer rpm (ω).

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* The Armco iron we used originally had the shape of round rods 12 mm in diameter; in preparing the plates these rods were first flattened out on an anvil, after which the plates were given a rectangular form by means of a file. The surface was given a final treatment with fine glass paper.

2. Variation of the solution rate and of the potential of dissolving iron with the dissolution time. The curves illustrating these functions are given in Figs. 1-4. In these figures, the iron dissolution time, reckoned from the instant the metal was immersed in the solution, is plotted along the axis of abscissas. The values of the dissolution rate, $v \cdot 100$, and the potential of the dissolving iron are plotted along the axis of ordinates.

In all the figures the potential curves are denoted by digits with a prime ('), the solution rate curves being denoted by digits without a prime. Figure 1 illustrates the dissolution of light sheet iron in hydrochloric acid, Curves 1 and 1' representing the dissolution of the light sheet iron in 3.5 N hydrochloric acid, while Curves 2 and 2' represent its dissolution in 10 N hydrochloric acid. Inasmuch as the rate at which iron dissolves in the 10 N hydrochloric acid is much higher than the solution rate in the 3.5 N acid, different scales are employed for Curves 1 and 2 in Fig. 1. The solution rates are laid off as ordinates at the left for Curve 1, those for Curve 2 being laid off at the right; similarly, the scale for Curve 1 is laid off in hours along the axis of abscissas, while that for Curve 2 is laid off in minutes. Figure 2 gives the curves for two tests of the dissolution of the same light sheet iron in sulfuric acid, Curve 1 representing a test in 2 N sulfuric acid, while Curve 2 shows a test using 8 N sulfuric acid. The curves in Fig. 3 illustrate the dissolution of Armco iron in hydrochloric acid, while the curves in Fig. 4 show the behavior of the same Armco iron in sulfuric acid. When we inspect Figs. 1 and 2, we see that a constant rate of solution is not established at once when light sheet iron is dissolved in hydrochloric or sulfuric acid. At the start of the test there is a characteristic induction period, during which the solution rate rises. The potential of the dissolving light sheet iron, on the other hand, drops during this period by about 20-30 millivolts. Hence, at the beginning of the test, the potential and the rate of solution of light sheet iron move in opposite directions. It might also be noted that in the test represented by the Curves of Fig. 2, the dissolution of the light sheet iron was effected at various stirring speeds, to wit: at $\omega = 550$ rpm to begin with, then at $\omega = 0$, and again at $\omega = 550$ rpm toward the end of the run. The curves of Fig. 2 indicate that a change in the rate at which the solution is stirred has no perceptible effect upon the rate at which light sheet iron dissolves in sulfuric acid or upon its potential. In general, we may state that the state of affairs observed in the dissolution of light sheet iron in hydrochloric acid as well as in sulfuric acid is comparatively simple. The behavior patterns

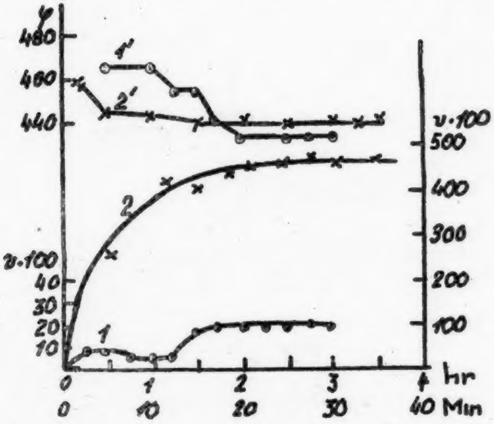

Fig. 1.

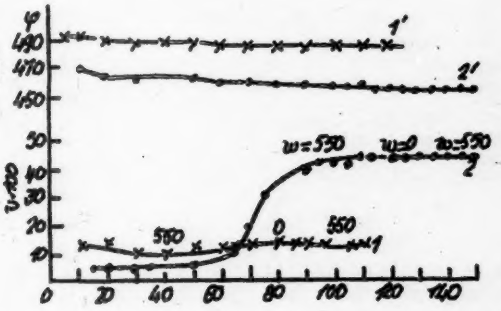

Fig. 2.

exhibited by the Armco iron are more complex.

In Fig. 3, Curve 1 represents a test of the dissolution of Armco iron in 9 N hydrochloric acid, Curve 2 representing its dissolution in 7.5 N hydrochloric acid, and Curve 3 representing its dissolution in the same 7.5 N hydrochloric acid, but at 50°. The curves in Fig. 3 indicate that the length of the induction period may vary very widely for the dissolution of Armco iron in hydrochloric acid, the variation being independent of the acid concentration. Curve 3, for example, exhibits an induction period of the order of 20-30 minutes; in the test represented by Curve 2 the induction period was still shorter; in the test represented by Curve 1, on the other hand, the induction period was very long, some 3 hours, despite the high acid concentration. (The time values laid off on the axis of abscissas must be multiplied by two for this curve.)

When we turn to sulfuric acid, the state of affairs prevailing in the dissolution of Armco iron becomes much more complicated. When Armco iron is dissolved in sulfuric acid, the rate of solution drops rather than rises at the start of the test. It usually reaches a constant value after a certain interval of time has passed, but the curve is hard to reproduce. In some tests the solution rate seemed to reach a constant value, but then it suddenly began to drop, falling to zero. Curve 1 in Fig. 4 represents a test of this sort. Curve 2 in that figure represents a test in which no such drop was observed.

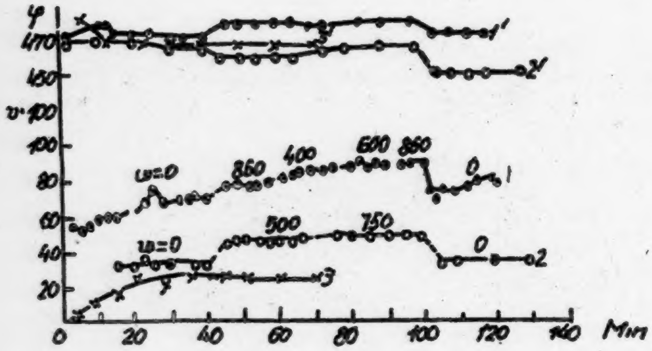

Fig. 3.

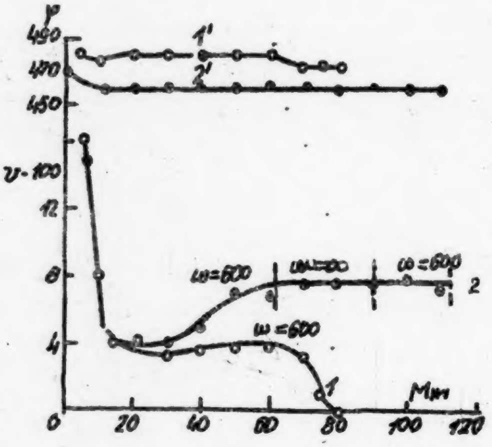

Fig. 4.

It should likewise be observed that the sulfuric acid concentrations were fairly close in the tests represented by Curves 1 and 2 in Fig. 4, being 10 N for Curve 2 and 9 N for Curve 1, which clearly proves that the rate at which the Armco iron dissolved was greatly diminished in the test represented by Curve 1. Thus, phenomena resembling passivation are observed in the dissolution of Armco iron in sulfuric acid, though these phenomena do not involve corresponding abrupt changes in the potential of the dissolving metal. As Curve 2 in Fig. 4 indicates, stirring the solution has no appreciable effect upon the rate of dissolution or upon the potential of the Armco iron as it dissolves in sulfuric acid.

3. Temperature coefficient of the rate at which iron dissolves. The data on the temperature coefficient of the rate of solution of iron are listed in Table 1 and 2, Table 1 referring to the dissolution of Armco iron in hydrochloric acid,[*] while Table 2 gives the data for the dissolution of light sheet iron in

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[*] The temperature coefficient of the rate at which Armco iron dissolves in sulfuric acid was not determined because of the poor reproducibility of our data from the rate solution of Armco iron in sulfuric acid discussed above.

sulfuric acid. In these tables, C denotes the acid concentration; E is the critical increment of the solution rate; α% is the temperature coefficient of the solution rate, expressed in per cent per degree; v_{t+10}/v_t is the ratio of the solution rates at t + 10° and t°. The values given in these tables for the solution rates at 60° are taken from the curves in Figs. 5 and 6, while the values for the rates at 40, 50, and 70° represent data obtained in special tests.

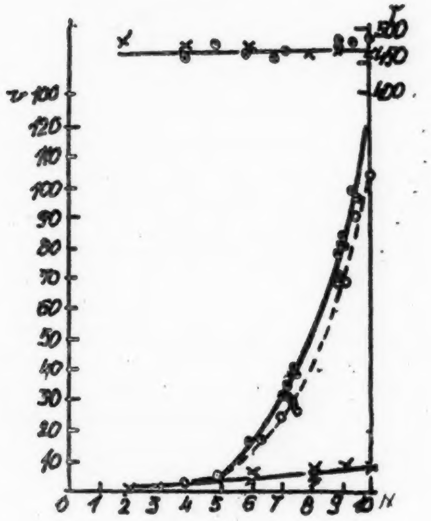

Fig. 5.

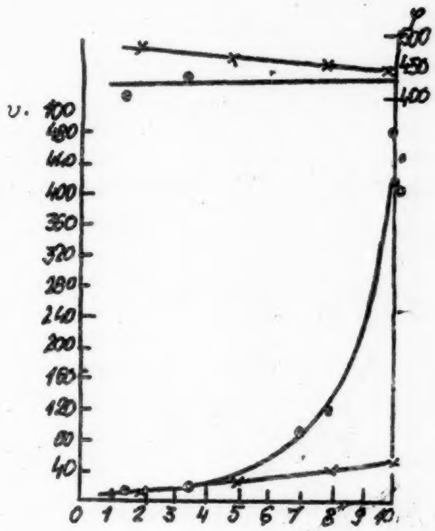

Fig. 6.

TABLE 1

Temperature Coefficient of the Rate of Solution of Armco Iron in HCl

1	2	3	4	5	6	7	8
C	t°	ω	v·100	E	α%	v_{t+10}/v_t	φ_{mv}
9.1	60°	600	80	13200	6.4	1.91	470-480
	40	600	22.1				470
7.5	60	600	38.1	13000	6.3	1.85	470
	50	600	21.0				468
6.0	60	600	15.0	13000	6.3	1.85	470
	50	600	8.1				460

The data in Table 2 indicate that the temperature coefficient of the rate at which light sheet iron dissolves in sulfuric acid is a typical value for the temperature coefficient of the rate of a chemical reaction. The temperature coefficient of the rate at which Armco iron dissolves in hydrochloric acid is somewhat lower, but it is still rather far from the temperature coefficient of processes whose rate is governed by the rate of the diffusion process. Column 8 in Tables 1 and

TABLE 2

Temperature Coefficient of the Rate of Solution of Light Sheet Iron in H_2SO_4

1	2	3	4	5	6	7	8
C	t°	ω	v·100	E	α%	v_{t+10}/v_t	φmv.
8	60	550	42.5	16.800	7.9	2.2	455
	50	550	19.2				460
2	60	550	12.4	19.500	8.5	2.3	487
	70	550	28.5				487

2 gives the values of the potential of the iron dissolving at the given temperature. The figures in this column indicate that the potential of the dissolving iron, measured against a saturated calomel electrode, hardly varies with temperature, the fluctuations lying within the limits of experimental error. It may be said that the drop in potential corresponding to a temperature drop of 10° seems to be roughly 10 millivolts.

4. Effect of stirring the solution upon the rate at which iron dissolves in hydrochloric and sulfuric acids. As we stated during our discussion of Figs. 2 and 4, the rate of solution of iron – both the Armco iron and the light sheet iron – in sulfuric acid is wholly independent of the rate at which the solution is stirred. A slight effect of the stirring rate upon the solution rate of the iron was observed, however, in the hydrochloric acid. Table 3 illustrates the extent of this effect.

TABLE 3

	C	ω rpm/min			
		0	400	600	800
Armco iron	4.0	2.3	–	–	2.3
	5.0	5.5	–	–	4.8
	7.2	29	34	–	34
	9.1	68	81	83	80
	9.9	103	117	--	117
Light sheet iron	3.5	19.5	19.5	–	–
	10	(400)	(405)	(445)	–

The first column of this table gives the concentrations of the hydrochloric acid, the others giving the rate at which the iron dissolves in this acid at the stirrer rpm, ω , given in the top line. We see from this table that at high concentrations of hydrochloric acid, 7 N and more, stirring the solution increases the rate of solution of the Armco iron slightly. This inccrease in the rate is so slight, however, that the only thing we can remark with any certainty is a difference in the rates of solution between stirring and the absence of any stirring, this change in the rate totaling only 10-15%.

Such a change in the rate is close to the magnitude of experimental error; it may be noted, however, when we compare the solution rates obtained at different values of ω during a single test. In the case of Armco iron, all the figures in Table 3 that lie on the same horizontal line represent the data secured in a single test. Curves 1 and 2 in Fig. 3 represent tests of this sort (the effect of stirring was somewhat more than usual in the test represented by Curve 2).

With the light sheet iron, it was only at moderate concentrations of hydrochloric acid that we were able to measure the solution rate at various values of ω in a single test; as Table 3 indicates, the rate at which light sheet iron dissolved was not affected by the stirring rate. In concentrated solutions of hydrochloric acid the plates of light sheet iron dissolved too fast for us to be able to measure the rate of solution at more than one value of ω in any single test. When we compared the rates of solution of light sheet iron in 10 N HCl, as obtained in different tests at different values of ω, we found that the rate increased somewhat as ω was raised, as is seen in Table 3. It is possible, however, as we just said, that this effect is the result of nothing but the experimental error. In any case we may state that here, too the effect of stirring, if any, is extremely small.

5. Variation of the rate of solution and of the potential of the dissolving iron with the concentration of hydrochloric and sulfuric acid. The curves representing these functions are shown in Figs. 5 and 6, the curves shown in Fig. 5 representing the dissolution of Armco iron, while the curves in Fig. 6 represent the dissolution of light sheet iron.

Inspection of these curves demonstrates that the rate of solution of the Armco iron and of the light sheet iron rises very rapidly with the concentration of hydrochloric acid, being a modulus, as it were, of this concentration. In the case of sulfuric acid, the increase in the rate of iron solution with the acid concentration is much slower, the rate of dissolution being close to a linear function of the acid concentration. Hence, the underlying nature of the variation of the rate of solution with the concentration of hydrochloric or sulfuric acid is the same in the dissolution of iron as in the dissolution of chromium. Moreover, it must be remembered that in plotting the curve representing the rate at which chromium dissolves as a function of the concentration of sulfuric acid, we found that the curve is slightly convex downward, thus departing from strict linearity. Figure 6 seems to indicate that a similar phenomenon is present in the dissolution of light sheet iron.

In the case of Armco iron, the reproducibility of our results was unsatisfactory for the rate of solution in sulfuric acid, as we have said, so that our only recourse was to draw an approximate straight line, as is shown in Fig. 5. It should be added that we have plotted two curves in Fig. 5 for the dissolution of Armco iron in hydrochloric acid: the solid curve, representing the dots, and the dotted curve, representing the circles. The dotted curve represents the tests made without stirring, at $\omega = 0$, while the solid curve represents the experiments in which stirring was employed.

We see that in both cases we get a curve of the same type; the two curves nearly coincide at hydrochloric acid concentrations below 5-6 N. At higher concentrations the dotted curve is somewhat below the solid one, but this drop is insignificant, averaging some 10-15%. (These facts are, of course, merely a paraphrase of the statements made earlier, in Par. 4). The fact that stirring influences the rate at which iron dissolves in hydrochloric acid enables us to assume that the diffusion process has some influence upon the rate of this reaction. This influence is evidently very small, however, practically disappearing at a rather low stirring rate. In support of this conclusion we may also point out that experiments on the rate of solution of magnesium made by us in similar instruments [10] have shown that the rate at which magnesium dissolves rises about 300% as the stirrer speed is increased from zero to 700 rpm, whereas the change in the rate of solution of iron is only 10-15%.*

This conclusion is also supported by the high temperature coefficient of the rate at which iron dissolves.

The values of the rate at which iron dissolves ($v \cdot 100$) in hydrochloric and sulfuric acids of various concentrations are listed in Table 4, obtained by interpolation from the curves reproduced in Figs. 5 and 6.

In accordance with what was set forth on Page 672, the figures obtained

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*We regard the dissolution of magnesium in hydrochloric acid as a typical example of a reaction in which the factor governing the reaction rate is the diffusion process.

TABLE 4

Normality of the acid		1	2	3	4	5	6	7	8	9	10
		$\underline{v}\cdot 100$									
Armco iron	HCl	–	–	–	2.3	5.5	15	30	50	77	120
Light sheet iron	HCl	8.0	13(5)	17	24	36	56	85	135	230	430
Armco iron	H_2SO_4	–	(1.8)	–	(3.0)	–	(4.5	–	(6.4)	–	(8.0)
Light sheet iron	H_2SO_4	–	12(5)	16	20	25	30	35	40	46	52

for the rate at which Armco iron dissolves in sulfuric acid fluctuated widely, so that the values given in the table for the rate of solution of Armco iron in sulfuric acid are placed in parentheses, as being merely approximate. Nonetheless, it is obvious that the rate at which Armco iron dissolves in sulfuric acid as well as in hydrochloric acid is much lower than the rate of solution for light sheet iron. The potential of the iron dissolving in hydrochloric and sulfuric acids at different concentrations are given at the top of Figs. 5 and 6, the potentials of iron dissolving in hydrochloric acid being indicated by dots, while those for dissolution in sulfuric acid are shown by crosses. The data in Fig. 5 indicate that the potential of Armco iron varies very little with the acid concentration. The potential of the light sheet iron in sulfuric acid drops slightly as the acid concentration is increased.

We have a total of three points for the potential of light sheet iron in hydrochloric acid, their positions not permitting us to make any definite statement regarding the variation of this potential with the acid concentration. By analogy with the potential of Armco iron, it may be thought that this potential is close to a constant (the horizontally aligned dots shown in Fig. 6).

For the sake of greater clarity, the variation of the potential of dissolving iron with the acid concentration is shown on a larger scale in Fig. 7 (A, B, C). Fig. 7(A) represents the dissolution of light sheet iron in sulfuric acid; Fig. 7(B) represents Armco iron in sulfuric acid; and Fig. 7(C) represents Armco iron in hydrochloric acid. The potentials of the dissolving iron at the beginning of the test are denoted by circles, the crosses denoting the potentials at the end of the test. Figure 7 shows that the difference between the initial and the final values of the potential is much greater for light sheet iron. In sulfuric acid, the potential of dissolving iron, whether light sheet or Armco iron, drops somewhat as the acid concentration increases, the drop being biggest for the potential of light sheet iron as measured at the end of the tests, this drop totaling some 45-50 millivolts, according to Fig. 7(A), between 2 $\underline{N}$ and 10 $\underline{N}$ sulfuric acid. The decrease in the initial values of the potential of light sheet iron during the same concentration range is smaller – of the order of 20 millivolts. As we see in Fig. 7(B), the potential of Armco iron in sulfuric acid drops by about the same amount, though the difference between the initial and final values of the potential is much smaller than in the case of the light sheet iron.

When Armco iron is dissolved in hydrochloric acid, Fig. 7(C), the difference between the initial and terminal values of the potential is again small. In view of the fairly high scattering of the points in Fig. 7(C), we may take the potential of iron dissolving in hydrochloric acid to be a constant, equaling $\varphi =$ $= 0.47 \pm 0.01$ v. Here too, however, as in the potential of chromium dissolving

TABLE 5

Acid	Potential of Armco iron, mv.	Potential of light sheet iron, mv
H_2SO_4	475	465* 480°
HCl	472	430* 460°

in hydrochloric acid, there is an apparent tendency for the potential to rise somewhat as the acid concentration is increased, as is indicated roughly by the dotted straight line in Fig. 7(C). In general, we see that the behavior of the potential of dissolving Armco iron is rather much like that of the potential of dissolving chromium.

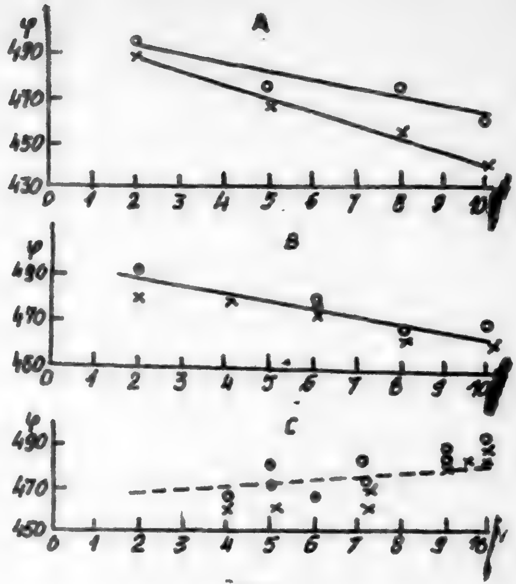

Fig. 7.

The values of the potential of dissolving iron in a 6 N acid are listed in Table 5 for the sake of comparison. In this table the potentials of light sheet iron are indicated by an asterisk for the start of the run, and by a degree mark (°) for the end of the run. The differences between the initial and terminal potentials of Armco iron were insignificant, so that a single mean value is given in Table 5 for the potential of Armco iron.

We see in Table 5 that the mean values of the potential of Armco and light sheet iron in hydrochloric and sulfuric acids are fairly close together, so that they may all be covered by a single expression, $\varphi = 0.47 \pm 0.01$ v. The sole exception is the potential of light sheet iron in hydrochloric acid at the end of the tests, the value of which was lower: ca. 0.43 volt.

Taking the potential of the calomel electrode with respect to the reference hydrogen electrode as 0.221 volt at 60°, we get a value of 0.25 volt for the potential of dissolving iron, measured against the reference hydrogen electrode, but with a plus sign.

SUMMARY

1. The rate of solution of Armco iron and of commercial light sheet iron in hydrochloric and sulfuric acids at 60° was investigated up to acid concentrations of 10 N.

2. The data on the effect of stirring upon the rate at which iron dissolves and on the temperature coefficient of this rate indicate that the rate of solution of iron in sulfuric or in hydrochloric acid may be regarded as practically independent of the effect of the diffusion process.

3. The rate at which Armco iron dissolves, whether in hydrochloric or in sulfuric acid, is much lower than the rate of solution for light sheet iron.

4. The rate at which Armco and light sheet iron dissolve in hydrochloric acid is an index to the concentration of the acid, the relationship being nearly a linear function in sulfuric acid, however, up to a 10 N concentration. Hence, the variation of the rate at which iron dissolves with the acid concentration (HCl and H_2SO_4) is analogous to the corresponding function described in our previous paper on chromium, the sole difference being, however, that the $\underline{v}$–C_{HCl} curve

for iron at $\omega = 0$ has no maximum, such as it had in chromium, exhibiting practically no difference from the curve obtained for vigorous stirring of the solution.

5. The potential of Armco iron in hydrochloric acid changes very little with the concentration of the acid. The potential of Armco iron in sulfuric acid drops somewhat as the acid concentration is increased, but this drop is small, amounting to some 20 mv in the range from 2 N to 10 N H_2SO_4. This drop is somewhat greater, ca. 45 mv, in the case of light sheet iron.[*]

6. The potential of Armco iron is practically the same in average 6 N concentrations of sulfuric or hydrochloric acids.

Measured with respect to a saturated calomel electrode and with its sign taken as plus, it amounts to 0.47 ± 0.01 volt; measured with respect to a reference hydrogen electrode and taken with a plus sign, it is 0.25 volt.

Inasmuch as the normal potential of iron is 0.44 volt, it is evident that the dissolution of iron, like that of chromium, is accompanied by considerable anodic polarization.

It should be noted that the book by Gatty and Spooner [11] gives the potential of iron in 1 N hydrochloric and sulfuric acids as 0.27 volt in a table on p. 312-313, this figure being in close enough agreement with the values we have found.

The problem of the potentials of dissolving iron will be considered in greater detail in one of our forthcoming papers.

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[*] It should be borne in mind however, that the iron potential measured with respect to a saturated calomel electrode contains the potential jump at the boundary between the hydrochloric acid and the saturated solution of potassium chloride, which may vary with a change in the acid concentration. The feasibility of excluding the resulting difficulties from a theoretical treatment of the problem will be discussed in one of our forthcoming papers.

[**] See CB translation p. a-605 ff.

COORDINATION COMPOUNDS OF CADMIUM WITH AMMONIA AND SOME DERIVATIVES OF AMMONIA

I. A. Korshunov and L. V. Lipatova

Introduction. When ammonia is added to a solution containing cadmium ions, the hydroxide that forms at first is readily dissolved in the excess of precipitant, giving rise to complex ions in accordance with the equation:

$$Cd^{++} + pNH_3 \rightleftarrows Cd(NH_3)_o^{++}.$$

The value of p may vary, depending upon the concentration of ammonia in the solution. We decided to use polarographic analysis to gain a better idea of the composition of the complex ions formed in various concentrations of ammonia. A similar type of formation of coordination compounds occurs in solutions of cadmium salts to which some derivatives of ammonia have been added, such as monoethanolamine, triethanolamine, methylamine, and trimethylamine.

There is no detailed investigation in the literature dealing with the composition of the complex ions formed at various concentrations of the foregoing substances.

We were interested in filling the gap existing in the literature and in establishing the composition of coordination compounds of cadmium with various ammonia derivatives and in determining their instability constants. We employed the polarographic method of research in making these investigations as well.

Instrumentation. The diffusion currents were measured with a visual instrument. We utilized a tiny beaker, with a capacity of 15 ml, as the electrolytic cell containing the solution under test, into which a dropping mercury electrode of ordinary design was lowered. A saturated calomel half-cell was used as the nonpolarizing comparison electrode, its potential being assumed to be zero. All measurements were made in a thermostat at a temperature of $25.0 \pm 0.3°$. We did not get rid of the dissolved oxygen before making a polarographic record, since the oxygen diffusion currents did not interfere with the measurement of the cadmium diffusion currents. We prepared the initial 0.1 N solutions of cadmium sulfate and a 1.0 N solution of potassium sulfate for polarography, mixing them in the electrolyzer. The electrolyzer also contained the required quantity of the solution of ammonia, monoethanolamine, etc. A certain amount of water was also added to keep the concentration of cadmium ions constant.

We used salts of cadmium and potassium, methylamine and trimethylamine, marked "pure, for analysis", as our reagents. The monoethanolamine and the trimethanolamine contained water as an impurity, while the mono-, di-, and triethanolamine also contained up to 1.5% of ammonia.

EXPERIMENTAL

a) Complex ions of cadmium and ammonia. During the polarography of the solutions the concentration of cadmium ions was kept constant at 0.01 N, while the concentration of potassium chloride was likewise kept constant at 0.1 N; as for the concentration of ammonia, it was varied from 0.5 N to 4.0 N. As the ammonia concentration was increased, the cadmium halfwave potential was shifted toward more highly negative values.

The cadmium diffusion current remained constant and independent of the concentration of ammonia in the solution.

The cadmium diffusion currents are well defined, being described by the following equation for a polarographic wave:

$$\pi = \pi_{1/2} - \frac{2.3\,RT}{nF}\log\frac{i}{i_d - i}, \qquad (1)$$

where $\pi_{1/2}$ is the cadmium halfwave potential.

When plotted in $\pi - \log\frac{i}{i_d - i}$ coordinates, this equation is a straight line, the slope of which enables us to find the value of n, the number of electrons taking part in the reduction of the cadmium ions. According to our experimental results, this value was quite close to 2, i.e., in good agreement with the reduction of divalent cadmium ions at the surface of a dropping mercury electrode.

b) Complex ions of cadmium with mono- and triethanolamine. As the concentration of mono- and triethanolamine in the solution is increased, while the percentage of cadmium ions is kept constant, the cadmium halfwave potential shifts toward more highly negative values. This shift of the halfwave potential becomes perceptible at concentrations of mono- and triethanolamine totaling 1.2 N and higher.

The diffusion waves of cadmium diminish somewhat as the concentration of the ethanolamines increases. This decrease is most likely related to an increase in the viscosity of the polarographed solutions rather than to a retardation of the rate of dissociation of the complex ions that are formed. It should be noted that the cadmium diffusion currents are well reproducible in the presence of mono- or triethanolamine and are quite satisfactory for quantitative measurements.

The diffusion wave is described by the equation for the polarographic wave cited above, as was the case in the reduction of the cadmium ions in the presence of ammonia. According to our results, the coefficient of the logarithmic term was 1.8, which agrees satisfactorily with the theoretical value for a two-electron process.

c) Complex ions of cadmium and methyl- or trimethylamine. In this series of experiments the concentrations of methylamine and trimethylamine ranged from 0.5 N to 6.3 N and from 0.5 N to 5.0 N, respectively.

It should be pointed out that the shift in the cadmium halfwave potential took place at concentrations of 0.5 N and up to methylamine or trimethylamine. At concentrations below 0.5 N the shift in the halfwave potential was so slight as to justify the assumption that no complex ions are formed in the solution.

The polarograms yielded several cadmium diffusion currents of constant magnitude, irrespective of the concentration of the monomethyl- or trimethylamine in the solution. All our experimental results are reproduced graphically in the figure as the variation of the halfwave potential of the reduction of cadmium with the logarithm of the concentration of ammonia, monoethanolamine, triethanolamine, monomethylamine, and trimethylamine.

Evaluation of Results

The shift of the halfwave potential during the formation of complex ions is governed by the equation:

$$(\pi_{1/2})_k - (\pi_{1/2})_2 = \frac{2.3}{nF}\log K_c - \frac{2.3\,RT}{nF}\log C, \qquad (2)$$

whence:

$$\frac{d\pi_{1/2}}{d \log C} = - p \, \frac{2.3 \, RT}{nF}. \tag{3}$$

Inspection of the curve indicates that the relationship between the cadmium halfwave potential and the ammonia concentration may be represented by two equations:

for ammonia concentration below 0.9 N,

$$\pi_{1/2} = - 0.870 - 0.088 \log C_{am}. \tag{4}$$

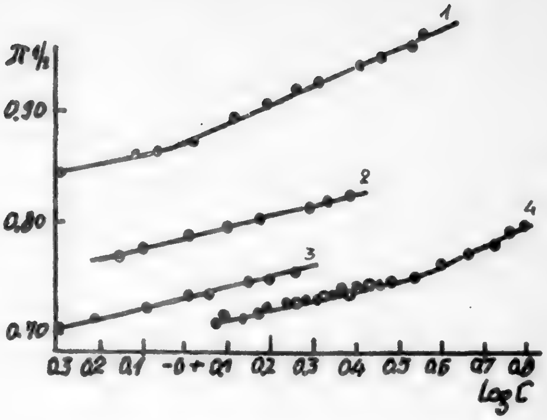
and for ammonia concentrations above 1.0 N,

$$\pi_{1/2} = - 0.874 - 0.180 \log C_{am}. \tag{5}$$

In the reduction of cadmium from solutions containing monoethanolamine, the following equation applies:

$$\pi_{1/2} = - 0.785 - 0.095 \log C. \tag{6}$$

where C is the concentration of monoethanolamine in the polarographed solution.



The cadmium halfwave potential as a function of the logarithm of the concentration of ammonia (1), monoethanolamine (2), triethanolamine (3), and mono- and trimethylamine (4).

In the formation of complex ions in solutions containing triethanolamine, this equation becomes:

$$\pi_{1/2} = - 0.732 - 0.093 \log C. \tag{7}$$

In methylamine solutions there are two coordination compounds, apparently.

At concentrations of mono- and trimethylamine ranging from 1.2 N to 3.5 N, the relationship between the cadmium halfwave potential and the concentration of the methylamines is given by the equation:

$$\pi_{1/2} = -0.700 - 0.09 \log C \tag{8}$$

while the corresponding equation for methylamine concentrations ranging from 3.5 to 6.0 N is:

$$\pi_{1/2} = -0.650 - 0.180 \log C. \tag{9}$$

The coordination number and the possible composition of the complex ions are readily found from these equations.

In ammonia solutions, the concentration of which ranges from 0.6 N to 0.9 N, a complex ion containing 3 molecules of ammonia is formed. But the complex ion contains 6 molecules of ammonia when the ammonia concentration ranges from 1.0 N to 4.0 N. It is not impossible that complex ions of different composition are formed at ammonia concentrations of 0.9 N to 1.0 N or else the concentration of the $Cd(NH_3)_3^{++}$ complex ion is diminished while that of the complex ion $Cd(NH_3)_6^{++}$ is increased. In solutions of the mono- and trimethylamine the composition of the complex ions remains the same throughout the tested range of concentrations of the monomethylamine or the trimethylamine. In this case, the complex ions that are formed have three molecules of the mono- or the trimethylamine, i.e., their composition is $Cd(NH_2CH_2CH_2OH)_3^{++}$ or $Cd[N(CH_2CH_2OH)_3]_3^{++}$.

The complex ion contains three molecules of the mono- or triderivative of ammonia when monomethylamine or trimethylamine is present and the concentrations of the latter vary from 1.2 N to 3.5 N. At concentrations in excess of 3.7 N, the coordination number of the ions formed is 6.

In the intermediate region of concentrations, from 3.5 N to 3.7 N, it is possible that complex ions of different composition are formed or that the concentration of the complex ion with a coordination number of 3 diminishes while that of the complex ion with a coordination number of 6 is increased. Our polarographic investigations cannot give an unequivocal answer to this question. If we assume that complex ions with a coordination number of 4 are possible, however, it must be borne in mind that the range of concentrations of ammonia or of the methylamines in which they may predominate in the solution is very restricted.

Equation (2) may be utilized to compute the instability constants of the ions formed:

$$K_c = \frac{[Cd^{++}][NH_3]^p}{[Cd(NH_3)_p{}^{++}]} . \qquad (10)$$

The brackets denote the concentrations of the end products of dissociation rather than dissociated ions. The dissociation of complex ions takes place in stages, to be sure; the calculated overall constant gives us an idea, however, of the relative stability of the resultant ions.

For complex ions of cadmium and ammonia, with coordination numbers of 3 and 6, the calculations yield $K_c = 2.4 \cdot 10^{-8}$ and $K_c = 1.7 \cdot 10^{-9}$.

According to our measurements, the halfwave potential of cadmium in the presence of a solution of 0.1 N potassium chloride is − 0.62 volt. The instability constant of the complex ion of cadmium and monoethanolamine is $K_c = 2.04\ 10^{-6}$, and that of its complex ion with triethanolamine is $K_c = 1.38 \cdot 10^{-4}$.

The instability constants are identical for the complex ions of cadmium with mono- and trimethylamine formed in solutions of the latter at concentrations of 1.2 N to 3.5 N, being $K_c = 1.74 \cdot 10^{-3}$. For complex ions of cadmium with the formulas $Cd(NH_2CH_3)_6{}^{++}$ and $Cd[N(CH_3)_3]_6{}^{++}$, $K_c = 9.3 \cdot 10^{-2}$.

Thus, the ammonia coordination compounds of cadmium are most stable. The numerical values of the instability constant of complex ions of different composition do not differ very much. The stability of complex ions of cadmium and the ethanolamines is lower than that of the ammonia complex ions. Complex ions with monoethanolamine are more stable than those containing triethanolamine We have been unable to observe the formation of any complex ions of cadmium with mono- or triethanolamine possessing a coordination number of 6. When the concentration of mono- or triethanolamine in the polarographed solutions exceeds 2.5 N, the viscosity of the solution increases quite appreciably; as a result the cadmium diffusion currents diminish, and the measurement results cannot be utilized for subsequent computations.

Of all the complex ions tested, the least stable are the complex ions of cadmium and the methylamines, their stability being rather negligible. It is worthy of note that the same coordination numbers hold good for the complex ions of cadmium with monomethylamine and trimethylamine, i.e., 3 and 6, as for its complex ions with ammonia. Inasmuch as the stability of the complex ions with the methyl derivatives of ammonia is much less than that of the complex ions with ammonia itself, they are formed in solutions with higher concentrations of monomethylamine or trimethylamine.

SUMMARY

1. A study has been made of the reduction of cadmium ions in ammonia,

monoethanolamine, triethanolamine, monomethylamine, and trimethylamine, it being found that complex ions are formed in these solutions.

The composition of the resulting complex ions depends upon the concentration of the ammonia, monoethanolamine, triethanolamine, etc.

2. It has been found that complex ions with coordination numbers of 3 and 6 are formed. The ammonia complex ions of cadmium are the most stable, while the methylamine complex ions are the least stable.

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POLAROGRAPHIC INVESTIGATION OF COORDINATION COMPOUNDS OF CADMIUM WITH SEVERAL MONOVALENT ANIONS

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Introduction. What is quite characteristic of some salts of cadmium is their tendency to form coordination compounds, say, in the reaction:

$$3CdI_2 \rightleftarrows Cd(CdI_3)_2 \rightleftarrows Cd^{++} + CdI_3^{--},$$

greatly diminishing the concentration of hydrated cadmium ions in the solution. Coordination compounds are also formed in solutions containing alkaline salts of halogen acids or containing free acids. The composition of the complex ions and their stability depend upon the concentration of the anions of the hydrochloric, hydrobromic, and hydriodic acids and upon the composition of the solution. The well-known relationship of the halfwave potential of reduction of metallic ions to the instability constant of the complex ions and the concentration of the solution in which the complex ions are formed may be utilized to determine the composition of the resultant complex ions.

This relationship is given by Equation (1):

$$(\pi_{1/2})_k - (\pi_{1/2})_g = \frac{2.3 \cdot RT}{nF} \log K_c - p \frac{2.3 \cdot RT}{nF} \log C \cdot \underline{f}, \qquad (1)$$

where $(\pi_{1/2})_k$ is the reduction potential of the metal in the complex ion; $(\pi_{1/2})_g$ is the reduction potential when the central atom of the complex ion is present; K_c is the instability of the resulting complex ions; $\underline{p}$ is the coordination number; $\underline{C}$ is the concentration; and $\underline{f}$ is the activity coefficient of the ions constituting the inner sphere of the coordination compound.

In accordance with the foregoing equation we may compute the coordination number of the coordination compound from the following formula:

$$\frac{d(\pi_{1/2})_k}{d \log C \cdot \underline{f}} = - p \frac{2.3 \cdot RT}{nF}. \qquad (2)$$

In the present research we have determined the coordination numbers of coordination compounds of cadmium in solutions of potassium iodide and bromide, potassium chloride, ammonium thiocyanate, and hydriodic, hydrobromic, and hydrochloric acids.

Apparatus and experimental procedure. The apparatus required for measuring the diffusion currents and the reduction halfwave potentials, as well as the procedure involved in polarographic measurements, have been described by us previously [2].

The salts used in our measurements – cadmium sulfate, potassium chloride, sodium chloride, potassium iodide, potassium bromide – and the hydrochloric acid were all of the "pure, for chemical analysis" grade. We synthesized the hydriodic and hydrobromic acids by decomposing phosphorus bromide and iodide with water [1].

The concentration of cadmium sulfate in the polarographed solutions was kept constant at $1 \cdot 10^{-3}$ N. The concentrations of the potassium iodide and hydriodic acid were varied from 0.05 N to 2.5 N, those of the potassium bromide and the hydrobromic acid from 0.5 N to 5.0 N, that of the sodium chloride from 1.0 N to 4.0 N, that of the hydrochloric acid from 0.5 N to 6.0 N, and that of the ammonium thiocyanate from 0.5 N to 5.0 N. The oxygen was not eliminated from the solution, inasmuch as preliminary tests had shown that it did not interfere with the measurement of the diffusion currents and the halfwave potentials.

Experimental results. In our investigation of the reduction of cadmium ions from solutions containing chlorides, bromides, and iodides of the alkali metals, free halogen acids, and ions of thiocyanic acid, we found that the diffusion currents were readily reproducible and varied linearly with the concentration of the cadmium salt in the solution. At the same time, the diffusion current of cadmium remained constant in solutions with the above-mentioned concentrations of anions of the halogen acids and of thiocyanic acid. As the concentration was increased, the only factor that varied was the cadmium halfwave potential, which shifted toward more highly negative values.

A series of measurements was made to determine the influence of temperature upon the magnitude of the diffusion current. It was found that the cadmium diffusion current is a linear function of the rise in temperature of the polarographed solution, totaling 1.5% per degree. As for the cadmium halfwave potential, its changes were quite small in the temperature range from zero to 45°, lying well within the margin of experimental error.

The potential of the dropping mercury is related to the diffusion current by the following equation of the polarographic wave:

$$\pi = \pi_{1/2} - \frac{2.3\,RT}{nF} \log \frac{i}{i_d - i}. \qquad (3)$$

This equation is a straight line when plotted in the following coordinates: π, the potential of the dropping mercury electrode, and $\log \frac{i}{i_d - i}$, where i_d is the limiting diffusion current.

According to our experimental data, the coefficient of the logarithmic term in the foregoing equation is 0.028 for the reduction of cadmium from solutions containing its coordination compounds with anions of halogen and thiocyanic acids. This indicates that two electrons are consumed in the reduction of cadmium ions and the ensuing formation of a dilute amalgam, in accordance with the equation:

$$Cd^{++} + 2\,\underline{e} + Hg \rightleftarrows Cd(Hg). \qquad (4)$$

A perceptible shift of the cadmium halfwave potential toward more highly negative values takes place first in solutions of potassium iodide and hydriodic acid. This shift begins at concentrations of approximately 0.05 N and higher.

The shift of the halfwave potential takes place at concentrations in excess of 0.3 N solutions of the bromide and of hydrobromic acid, while it sets in at concentrations of 0.8 N in solutions containing chlorides or hydrochloric acid and at concentrations of about 0.4 N in solutions containing ammonium thiocyanate.

The variation of the halfwave potential of the reduction of cadmium with the activity of solutions of potassium iodide and bromide, sodium chloride, hydriodic acid, and ammonium thiocyanate is shown graphically in the figure. Some of our experimental data are listed in the table.

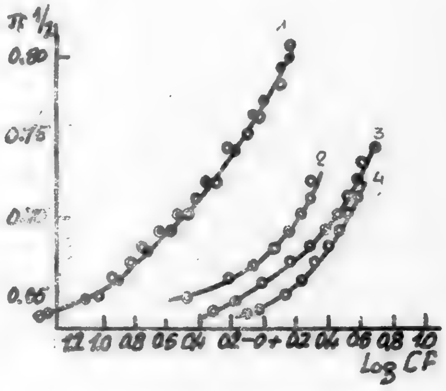
Evaluation of results. The curves in the figure indicate that there is no linear relationship between the halfwave potential of reduction of cadmium

TABLE 1

Cadmium Halfwave Potential in Various Electrolytes

Electrolyte	Concentration (gram-equivalents)							
	0.1	0.5	1.0	2.0	3.0	4.0	5.0	6.0
Potassium iodide ...	-0.652	-0.700	-0.747	-0.784	–	–	–	–
Potassium bromide ..	–	-0.65	-0.66	-0.68	-0.701	–	–	–
Sodium chloride ...	–	–	-0.637	-0.651	-0.670	-0.692	–	–
Ammonium thiocyanate	–	0.64	-0.66	-0.68	-0.70	-0.72	-0.74	–
Hydriodic acid	-0.64	-0.71	-0.76	-0.795	–	–	–	–
Hydrobromic acid ..	–	-0.65	-0.66	-0.70	-0.74	-0.76	–	–
Hydrochloric acid ..	–	–	–	–	-0.70	-0.72	-0.75	-0.79

and the concentrations of alkali salts and free halogen acids. Nor is there a linear relationship for solutions of ammonium thiocyanate. The curves do consist of several linear sections, however, of varying slopes.



Cadmium halfwave potential as a function of the solution activity.

1-Solutions of potassium iodide (circles) and hydriodic acid (dots), 2-potassium bromide; 3-ammonium thiocyanate; 4-sodium chloride.

Thus, the linear relationship between the halfwave potential and the concentration exists only within comparatively narrow ranges of measurements of the latter. This is evidence of the formation and existence of several complex ions of different composition within the solution, in equilibrium with one another. Each of these complex ions predominates within a given concentration range of any one salt or free acid.

The tangent of the angle of slope of the linear sections of the curve or of the tangents to the curve may be used to find the coordination numbers of the resulting complex ions from Equation (2). When Equation (2) is utilized to find the coordination number and when classifying our results, we must bear in mind that they must be integers. Values of the coordination number that are not integers indicate the presence of two or more complex ions with different coordination numbers.

Our experiments indicate that these integral values are 3, 4, and 6 for solutions of chlorides, bromides, and iodides of the alkali metals, ammonium thiocyanate, and hydriodic acid.

Complex ions of the same composition are formed at various concentrations of the salts and the free acids. A complex ion with the coordination number of 3 is formed, for example, in solutions of potassium iodide or hydriodic acid possessing concentrations of 0.13 N to 0.25 N, in solutions of potassium bromide at 0.8 N to 1.1 N, in solutions of ammonium thiocyanate at 0.6 N to 1.8 N, and in solutions of sodium chloride at 1.1 N to 1.7 N. Complex ions of cadmium with a coordination number of 4 are formed in solutions with concentrations of the iodine ion ranging from 0.3 N to 0.8 N, with concentrations of the bromine ion ranging from 1.2 N to 1.7 N, with concentration of the anion of thiocyanic acid ranging from 2.0 N to 3.1 N, and with concentrations of the chlorine ion ranging from 1.8 N to 2.5 N.

Complex ions with a coordination number of 6 are formed in solutions in which the concentration of anions of hydriodic acid is in excess of 0.9 N, that of anions of hydrobromic acid exceeds 1.8 N, that of anions of thiocyanic acid exceeds 3.2 N, and that of anions of hydrochloric acid exceeds 2.8 N. Hence, complex ions are formed at the lowest concentrations of iodine ions, followed by bromine and chlorine ions in that order.

It is highly probable that molecules and ions with coordination numbers of 2 and 1 are formed at low concentrations of the hydrohalides. When this is so, the solutions of the tested salts exhibit an equilibrium of the following type:

$$CdI_6^{=} \rightleftharpoons CdI_4^{--} + 2I^- \rightleftharpoons CdI_3^- + I^- \rightleftharpoons CdI_2 + I^- \rightleftharpoons CdI^+ + I^- \rightleftharpoons Cd^{++} + I^-.$$

Measurement of the potentials of the reduction of cadmium ions in various concentrations of hydrochloric acids indicates that complex ions are formed at about the same concentrations as when the alkali metal salts of these acids are used.

We were able to detect the formation of complex ions with a coordination number as high as 4 in free hydrobromic and hydrochloric acids. These complex ions are formed when the concentration of hydrobromic acid exceeds 1.4 N and that of hydrochloric acid exceeds 2.8 N.

The following equations may be written to express the variation of the halfwave potential of a dropping mercury electrode in the reduction of cadmium from solutions of hydrobromic acid with the activity of the latter:

$$\pi_{1/2} = -0.667 - 0.082 \log C_{HBr} \cdot f_{HBr}, \tag{4}$$

$$\pi_{1/2} = -0.654 - 0.119 \log C_{HBr} \cdot f_{HBr}. \tag{5}$$

The same relationship is expressed by the following equation for the formation of complex ions with a coordination number of 4 in solutions of hydrochloric acid:

$$\pi_{1/2} = -0.622 - 0.120 \log C_{HCl} \cdot f_{HCl}. \tag{6}$$

As we have stated above, Equation (1) may be utilized to find the instability constant of the resultant complex ions. This calculation requires that we know the half wave potential for the reduction of cadmium ions when no complex ion is formed.

Our measurements indicate that this equals -0.62 volt with respect to a saturated calomel electrode. The results of our computations are listed in Table 2. It should be borne in mind that these calculations cannot pretend to a high degree of absolute accuracy, owing to the error involved in the determination of the halfwave potential of cadmium ions, inasmuch as an inert electrolyte must be added to the solution when measuring the latter, and the cadmium halfwave potential depends somewhat upon the nature of the electrolyte. The

TABLE 2

Instability Constants of Complex Ions of Cadmium at a Temperature of 25°

Coordination number	Instability constant in solution of:						
	KI	HI	KBr	HBr	NaCl	HCl	NH_4CNS
3	$1.4 \cdot 10^{-4}$	$1.3 \cdot 10^{-4}$	$1.5 \cdot 10^{-2}$	$2.4 \cdot 10^{-2}$	0.17	–	$5.3 \cdot 10^{-2}$
4	$1.5 \cdot 10^{-5}$	$1.5 \cdot 10^{-5}$	$1.4 \cdot 10^{-2}$	$6.7 \cdot 10^{-2}$	0.45	0.85	0.86
6	$1.0 \cdot 10^{-6}$	$1.4 \cdot 10^{-5}$	0.11	–	1.09	–	1.03

figures in Table 2 give dependable notions of the relative stability of various complex ions.

The increasing stability of the complex ions in the series from Cl^- to I^- is readily seen. This increase in stability corresponds to the increase in the ionic radii of the anions and their polarizability. We note that the instability constant diminishes at the same time, so that the stability of complex ions increases in solutions of potassium iodide as the coordination number rises.

In contrast to this, the stability of complex ions in solutions of potassium bromide and sodium chloride diminishes as the coordination number is raised.

The decrease in the stability of complex ions in the series from I^- to Cl^-, probably due to a change in the forces of interaction among the ions, has as a result that any appreciable formation of coordination compounds requires an increasing concentration of the products of the dissociation of the coordination compounds, i.e., of the anions of hydrobromic and hydrochloric acids. The ions of thiocyanic acid, which likewise form coordination compounds with cadmium, yield ions whose stability is intermediate between those of the coordination compounds of cadmium with chlorine and iodine ions.

The numerical values of the instability constants for various coordination compounds of cadmium with anions of the halogen acids have been calculated [4] from measurements of the circuit emf:

$$\mathrm{Cd}\,|\,0.01 \text{ molar } CdSO_4\,|\,\text{satur. } KNO_3\,|\,\begin{matrix}0.01 \text{ molar } CdSO_4\\ x \text{ molar KHal}\end{matrix}\,|\,\mathrm{Cd},$$

where KHal denotes KI, KBr, or KCl.

The results agree fairly well with the figures we have derived, especially when the comments we have made above on the cadmium reduction potential in non-complex solutions are borne in mind.

Stromberg and Bykov [5] used the polarographic method of analysis to establish the composition of several coordination compounds of cadmium in solution. They found that the instability constant $K = 1.2 \cdot 10^{-6}$ for the complex ion CdI_4^{--}. This value is somewhat lower than the ones derived by us.

The stability of coordination compounds in free halogen acids is somewhat lower than the stability of the corresponding coordination compounds in hydrohalides. This may be due to the counterpolarization of the halogen ions entering into the composition of the coordination compounds by ions of hydrogen. As we know, this type of counterpolarization [3] by hydrogen ions results in a decrease in the stability of several oxy acids, such as H_2SO_3, HNO_2, etc., as compared with that of their salts.

SUMMARY

1. A study has been made of the reduction of cadmium ions at a dropping mercury electrode from solutions containing alkali metal salts of halogen acids, free halogen acids, and ammonium thiocyanate in various concentrations.

2. The coordination numbers of the resultant complex ions and their instability constants have been found from the shift of the halfwave potential of cadmium reduction.

3. It has been found that the composition of the resultant coordination compounds depends upon the concentration of the salts or of the free halogen acids. The stability of the complex ions depends upon their chemical composition and coordination number.

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* See CB translation p. 209 ff.

THE DISSOCIATION AND REDUCTION OF BARIUM AND CALCIUM PEROXIDES

B. D. Averbukh and G. I. Chufarov

In our preceding report [1], we compared the dissociation and reduction rates of silver oxide, this investigation resulting in an elucidation and confirmation of the adsorption-catalytic mechanism of the reduction of metal oxides.

The present paper, which is a continuation of the above-mentioned research, gives the results of an investigation of the dissociation and reduction of barium and calcium peroxides, which possess high dissociation pressures at comparatively low temperatures, and, therefore, are to be classed among the readily dissociated oxides.

Raw materials and experimental procedure. In our research we utilized peroxides of barium and calcium prepared by the reaction of hydrogen peroxide and ammonia with barium and calcium nitrates. The resulting precipitates were filtered out, washed with water, freed from CO_2, and desiccated for a month above calcium chloride and phosphoric anhydride.

The percentage of active oxygen in the peroxides, as determined by titration with a permanganate solution, is listed in Table 1.

TABLE 1

Percentage of Active Oxygen in the Original Samples

Name of sample	Percent of active oxygen by analysis	Theoretical percentage of active oxygen
BaO_2	7.6	9.44
CaO_2	18.23	22.2

The same apparatus and experimental procedure were used in investigating the rates of dissociation as in the preceding research [1]. The peroxides were reduced with hydrogen in a closed system, using circulation of the gas and elimination of water vapor by freezing in a trap immersed in liquid nitrogen. The reaction rate was measured by the drop in pressure in the system as a result of the consumption of hydrogen in the reaction.

Dissociation of barium and calcium peroxides. The rate of dissociation of barium peroxide was investigated in the temperature range of 500-750° and at oxygen pressures in the gas phase that ranged from a high vacuum to pressures approaching equilibrium, i.e., from $1 \cdot 10^{-3}$ mm Hg to 203 mm Hg for the given temperature range.

The results of a series of tests run to determine the variation of the rate of dissociation of BaO_2 with the percentage of oxygen in the solid phase are given in Fig. 1. The percent decomposition is laid off along the axis of abscissas, with the reaction rate, expressed in the amount of oxygen removed from the oxide in 30 minutes, laid off along the axis of ordinates. The amount of peroxide used was 0.3 g. The experiments were run at different oxygen pressures in the gas phase.

We see from Fig. 1 that the reaction rate rises as the oxygen pressure goes down. The variation of the rate of dissociation of the BaO_2 with the oxygen pressure at a constant percentage of oxygen in the solid phase is expressed by a straight line (Fig. 2), i.e., by the equation:

$$V_{diss.} = K(P_{O_2} - p_{O_2}),$$

in which $V_{diss.}$ is the dissociation rate of BaO_2; P_{O_2} is the equilibrium pressure of oxygen at the given temperature; and p_{O_2} is the oxygen pressure at which dissociation takes place.

The dissociation rate of calcium peroxide was investigated in the temperature range of 300-350°, at intervals of 10° and with the oxygen pressure in the gas phase ranging from 10 to 760 mm Hg.

The results of a series of tests made to determine the variation of the dissociation rates of CaO_2 with the percentage of active oxygen in the solid phase at various oxygen pressures in the gas phase are shown in Fig. 3. Inasmuch as these tests were made at pressures that were far from the equilibrium pressures (the equilibrium pressure of oxygen in the dissociation of CaO_2 is measured in hundredths of an atmosphere), the reaction rate did not differ at the different pressures. We see from Fig. 3 that the kinetics points plotted for different pressures all lie along the same straight line.

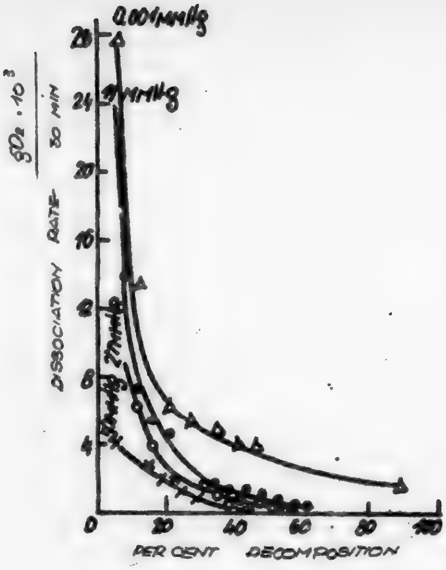

Fig. 1. Rate of dissociation of BaO_2 at 700°.

The apparent activation energies were determined from our experimental data on the change in the rate of dissociation of barium and calcium peroxides with temperature at a constant percentage of oxygen in the solid phase and a constant oxygen pressure in the gas phase. They were found to be 45,800 cal/mole for the dissociation of BaO_2 and 45,000 cal/mole for the dissociation of CaO_2.

The results of our investigation of the rate of dissociation of BaO_2 at various temperatures and oxygen pressure in the gas phase enabled us to determine the equilibrium pressure of oxygen in the dissociation of BaO_2 by extrapolating the straight lines in Fig. 2 to their intersection with the axis of abscissas, inasmuch as the dissociation rate is zero at equilibrium. The values given

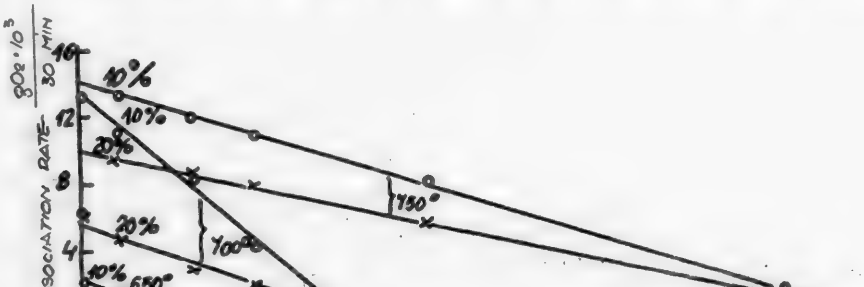

Fig. 2. Variation of the dissociation rate of BaO_2 with the oxygen pressure at various temperatures.

TABLE 2

Equilibrium Pressures of Oxygen in the Dissociation of BaO_2

Temperature, °C	Pressure, mm Hg
650	28
700	77
750	220

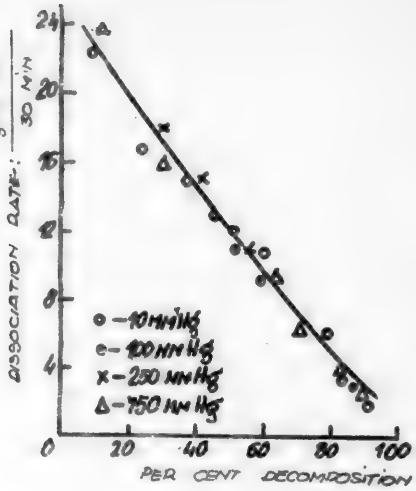

Fig. 3. Dissociation rate of CaO_2 at 350° for various oxygen pressures.

in Table 2 were obtained in this manner. Comparison of these figures with the data cited in the literature (Fig. 4) showed, however, that the equilibrium pressures of oxygen in the dissociation of BaO_2 differ greatly, depending on the author cited. The equilibrium pressures in the dissociation of BaO_2 that we have measured differ greatly from the values cited by M. Blumenthal [2], being fairly close to the values given by Hildebrand [3].

To clear up this matter, we made a direct determination of the equilibrium pressures of the dissociation of BaO_2 as a function of the percentage of active oxygen in the solid phase. The investigation was made by the static method, from the dissociation end as well as from the oxidation end.

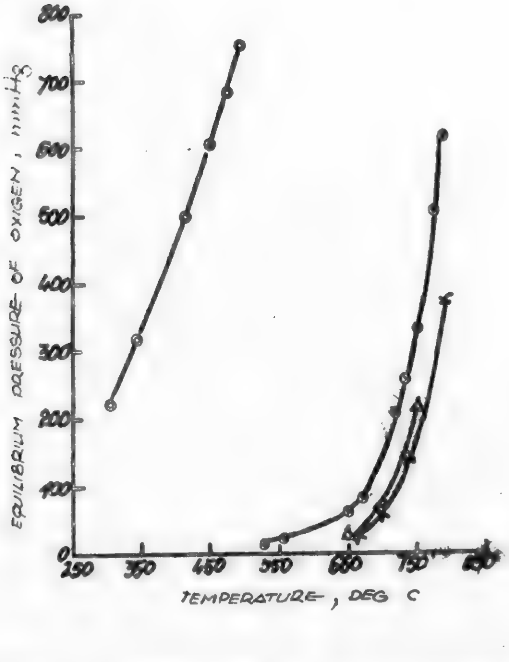

Fig. 4. Comparison of the equilibrium pressures of oxygen in the dissociation of BaO_2 according to various authors.

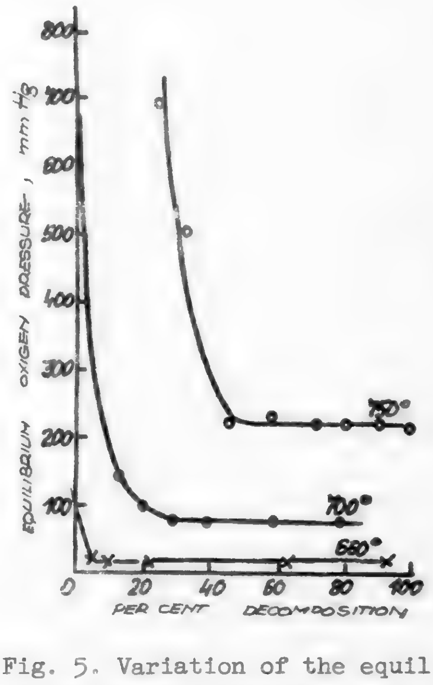

Fig. 5. Variation of the equilibrium oxygen pressure in the dissociation of BaO_2 with the percentage of active oxygen in the solid phase.

The change in the equilibrium oxygen pressure dissociation of BaO_2 is shown in Fig. 5 as a function of the percentage of oxygen in the solid phase for three different temperatures: 650°, 700°, and 750°. We see from this figure that when BaO_2 is dissociated we get univariant regions of solid solutions of limited solubility. The constant values of the equilibrium oxygen pressure obtained for each temperature in these regions are close to the values obtained in the kinetic tests.

These data enable us to set up the equation showing the variation of the equilibrium oxygen pressure during the dissociation of BaO_2 in the univariant region as a function of the temperature, making use of the thermodynamic equation in the first approximation:

$$\log P_{O_2}^{1/2} = \frac{-H_{298}}{4.573\ T} + \frac{S_{298}}{4.573} \ldots, \qquad (1)$$

where H_{298} is the standard heat of reaction at constant pressure; S_{298} is the standard entropy of the reaction; and T is the temperature in degrees Kelvin.

The value of the entropy for BaO_2 is unknown, so we computed it from Equation (1), using the experimental value of the equilibrium pressure in the dissociation of BaO_2 at 750°, 220 mm Hg or 0.29 atm, and the heat of reaction of 18.360 cal (according to the Landolt-Börnstein tables [4]).

Substituting these values in Equation (1), we get 16.71 cal/deg-mole as the entropy of the reaction $BaO_2 \rightleftarrows BaO + \frac{1}{2} O_2$. Since $S_{BaO} = 16.8$ cal/deg.-mole and $S_{O_2} = 49.02$ cal/deg-mole, we get $S_{BaO_2} = 16.8 + 49.02/2 - 16.71 = 24.6$ cal/deg-mole as the entropy of BaO_2.

Substituting the values of H_{298} and S_{298} in Equation (1), we get the following equation for the sought-for variation of the equilibrium dissociation pressure of BaO_2 in the univariant region:

$$\log P_{O_2}^{1/2} = \frac{-18,360}{4.573\ T} + 3.654. \qquad (2)$$

The equilibrium pressures in the dissociation of BaO_2, obtained by direct measurement, by extrapolation from the kinetic tests, and by computation from Equation (2), are compared in Table 3.

TABLE 3

Temperature	Temperature, °K	P_{O_2} (in mm Hg)		
		From kinetic tests	Measured	Calculated
650	923	28	21	30.9
700	973	77	77.5	86.9
750	1023	220	220	220

As we see from this table, the measured and calculated values of the equilibrium pressures in the dissociation of BaO_2 agree satisfactorily.

Reduction of barium and calcium peroxides. The reduction of the peroxides of barium and calcium by hydrogen at rather low temperatures involves the formation of hydrates in accordance with the following reaction:

$$BaO_2 + H_2 = Ba(OH)_2 \text{ and } CaO_2 + H_2 = Ca(OH)_2.$$

The experiments on the reduction of BaO_2 by hydrogen were made in the temperature range of 200-750°. The rate at which the BaO_2 is reduced increases as the temperature is raised, though the reaction is never complete, since the $Ba(OH)_2$ formed during the reduction fuses at 325°, and the molten $Ba(OH)_2$ coats the unreacted mass of BaO_2, impeding the access of hydrogen and causing the reaction practically to come to a stop.

Complete reduction is possible at temperatures in excess of 550°, owing to the dissociation of the $Ba(OH)_2$. $Ca(OH)_2$ is similarly formed in the reduction of calcium peroxide by hydrogen. At low temperatures – up to 320° – an extremely thin layer of $Ca(OH)_2$ is formed, retarding the further reduction of the peroxide. At higher temperatures, beginning at 320°, the CaO_2 can be reduced owing to the dissociation of the $Ca(OH)_2$ produced. Our experiments have shown that in the reduction of the peroxides of barium and calcium, all the hydrogen entering the reaction is used in forming the hydrate, water vapor not being generated in the gas phase (if the reduction temperature is low and the hydrates are not dehydrated). We checked this conclusion by means of special tests, in which the gas emerging from the reaction passed through a trap chilled by liquid nitrogen – if the reaction products had included water vapor, the latter would have condensed in the trap. No water vapor was ever found in our rather prolonged tests. This is evidence that the reaction takes place directly at the surface of the BaO_2 and the CaO_2, without any preliminary dissociation of the latter into oxygen and barium or calcium oxide, respectively.

Thus, the reduction of the peroxides of barium and calcium is not preceded by a primary dissociation into the oxide, followed by a union of the oxygen and the hydrogen in the gas phase, the reduction process taking place at the surface of the peroxide between the adsorbed hydrogen and the oxygen in the solid phase, giving rise to hydrates in accordance with the adsorption mechanism.

SUMMARY

An investigation has been made of the variation of the rate of dissociation of barium and calcium peroxides with the oxygen pressure in the gas phase. The rate is proportional to the difference between the equilibrium oxygen pressure P_{O_2} and its pressure p_{O_2} in the gas phase, provided the temperature and the per cent oxygen in the solid phase are held constant, i.e.:

$$V_{diss.} = K\,(P_{O_2} - p_{O_2}).$$

The apparent activation energy has been found to be 45,800 cal/mole for the dissociation of BaO_2 and 45,000 cal/mole for the dissociation of CaO_2.

The change in the equilibrium pressures during the dissociation of BaO_2 as a function of the percentage of oxygen in the solid phase is evidence of the formation of solid solutions in the Ba–O system, with limited solubility.

The variation of the equilibrium oxygen pressure with temperature in the univariant region is given by the equation:

$$\log P_{O_2}^{1/2} = \frac{-18,360}{4.573\,T} + 3.654.$$

The entropy S_{BaO_2} in this region has been found to be 24.6 cal/deg-mole.

When BaO_2 and CaO_2 are reduced by hydrogen at comparatively low temperatures, hydrates are formed, all the hydrogen entering into the reaction being used to form the hydrates, and no water vapor being evolved in the gas phase. This is evidence that the reduction process takes place solely at the surface of the peroxide, without any primary dissociation of the peroxide into the oxide and oxygen, which agrees with the adsorption-catalytic mechanism of the reduction process.

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THE HYDROLYSIS OF VINYL PHENYL ETHER

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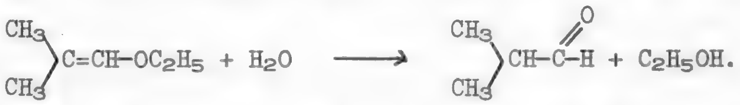
Of the known vinyl ethers produced by the Favorsky-Shostakovsky method, the one on which the least research has been done is vinyl phenyl ether. In connection with our research on the conditions required for the synthesis and transformations of α-halogen ethyl alkyl ethers [1,2] and α-halogen ethyl aryl ethers [3], we thought it necessary to make a study of the properties of the initial vinyl ethers, particularly the conditions governing the hydrolysis of vinyl phenyl ether.

As we know, the hydrolytic cleavage of vinyl alkyl ethers is an important reaction, enabling us to study the structure of the initial substances as well as the concentration of these compounds. A. Eltekov [4] was the first to hydrolyze substituted vinyl ethers with 1% sulfuric acid, as follows:



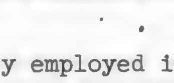
$$(CH_3)_2C{=}CH{-}OC_2H_5 + H_2O \longrightarrow (CH_3)_2CH{-}\overset{O}{\overset{\|}{C}}{-}H + C_2H_5OH.$$

In the subsequent researches of A.E.Favorsky [5], Wislicenus [6], and other authors, this reaction became a method of proving the structure of various α,β-unsubstituted ethers.

Lastly, the hydrolysis of vinyl alkyl ethers is widely employed in the laboratory and in industry [7] as a method for the quantitative determination of the original ethers. Besides this methodological importance, the hydrolysis reaction is of considerable practical value for the industrial production of acetaldehyde from vinyl ethers. This method, called the indirect hydration of acetylene, has been developed by M.F.Shostakovsky.

This reaction has attracted considerable attention in view of its great methodological and practical significance. The chemism and the kinetics of the hydrolysis of vinyl alkyl ethers have been the topics of papers by M.F.Shostakovsky and E.N.Prilezhaeva [7,8]. Up to the present time, however, no one has been able to discover the conditions required for the hydrolysis of vinyl phenyl ether. An attempt [9] was made to perform this hydrolysis under the conditions used for hydrolyzing the vinyl alkyl ethers, but it met with failure.

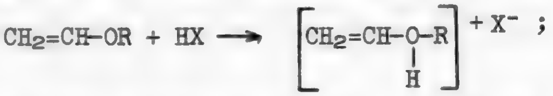
We have found that vinyl phenyl ether is hydrolyzed under conditions that are much more severe than those employed for the vinyl alkyl ethers. This agrees with the singularities of structure of the ether in question. The presence of the benzene ring in vinyl phenyl ether causes a polarization of its molecule (I) in which the oxygen loses its electron donor properties, thus interfering with the catalytic action of the HHal, where the hydrogen is an electron acceptor, as we know.



(I)

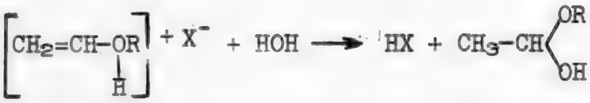
This is likewise borne out by the researches of I.P.Losev and his co-workers [10]; they noted the lower activity of vinyl phenyl ether with respect to the catalytic action of mineral acids in its polymerization processes. The mechanism suggested for the hydrolysis of vinyl ethers is the same as the mechanism for the hydrolysis of α-halogen ethers studied by us previously [11,12].

The hydrolytic cleavage of vinyl ethers takes place in the following stages: 1) formation of an oxonium coordination compound of the ether and the catalyst:



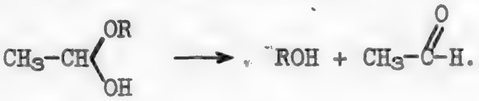
$$CH_2{=}CH{-}OR + HX \longrightarrow \left[CH_2{=}CH{-}\underset{\displaystyle H}{\underset{|}{O}}{-}R\right]^{+}X^{-};$$

2) Addition of water (hydration), resulling in the formation of a hemiacetal:



$$\left[CH_2{=}CH{-}\underset{\displaystyle H}{\underset{|}{O}}R\right]^{+}X^{-} + HOH \longrightarrow HX + CH_3{-}CH\left\langle\begin{matrix}OR\\OH\end{matrix}\right.$$

and 3) Cleavage of the resulting hemiacetal (the hydrolysis proper):



$$CH_3{-}CH\left\langle\begin{matrix}OR\\OH\end{matrix}\right. \longrightarrow ROH + CH_3{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}H.$$

We sought for the optimum conditions for hydrolyzing vinyl phenyl ether by raising the temperature and increasing the amount of catalyst used, as well as by making an investigation of the rate at which the acetaldehyde is formed; we determined the latter by bisulfite titration.

EXPERIMENTAL

We produced the original vinyl phenyl ether in the autoclave by the Favorsky-Shostakovsky method [9] from phenol and acetylene; its constants were as follows:

B.p. 155-156°; n_D^{20} 1.5225; d_4^{20} 0.9767; MR_D 37.46; computed 36.72.

The vinyl phenyl ether was hydrolyzed as follows: 20 ml of 2% H_2SO_4 and a weighed amount of vinyl phenyl ether were placed in a 100 ml ampoule; the ampoule was then sealed and immersed in a water bath, which was heated to boiling for 2 hours. After it had cooled, the ampoule's contents were transferred quantitatively to a 200-ml measuring flask; the solution was brought up to the mark by adding distilled water, the contents were thoroughly stirred, and then the percentage of acetaldehyde was determined. We added 15 ml of 0.3 N bisulfite to 50 ml of the test solution; the excess bisulfite was titrated back with 0.1 N iodine solution. The calculation was made from the following formula:

$$CH_3CHO = \frac{0.17348 \cdot 0.01269 \cdot 100\, M(b - c)}{44 \cdot a},$$

where a is the weight of vinyl phenyl ether used, in grams; b is the number of ml of 0.1 N iodine consumed in titrating the bisulfite used (blank test); c is the number of ml of 0.1 N iodine consumed in titrating the excess bisulfite; and M is the molecular weight of the vinyl phenyl ether. The table lists only a few of the large number of tests we have run. We see from the table that vinyl phenyl ether is most fully hydrolyzed by 2% sulfuric acid. It should also be stated that when the ampoules with the product to be hydrolyzed were not titrated immediately after heating, but 20 hours later, the per cent of titrated acetaldehyde was diminished when the 2% sulfuric acid was used, owing to the partial polymerization of the former.

Hydrolysis of vinyl phenyl ether with 1% H_2SO_4

Test No.	Weight of vinyl phenyl ether, grams	Dilution to	Quantity of solution used for titration, ml.	c	b	% CH_3CHO
9	0.5179	200 ml	50	27.10 27.10	45.30	84.41
10	0.5405	200 ml	50	24.95 24.90	43.80	84.00
12	0.9004	200 ml	50	12.10 12.00	43.80	84.57
Hydrolysis of vinyl phenyl ether with 2% H_2SO_4						
1	0.6050	200 ml	50	18.60 18.75	43.80	99.76
2	0.4155	200 ml	50	26.50 26.60	43.80	100.0
3	0.5747	200 ml	50	20.10 20.05	43.80	99.21

SUMMARY

A study has been made of the hydrolysis of vinyl phenyl ether, which resists the action of dilute mineral acids, and the optimum conditions for its hydrolytic cleavage have been determined.

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[*] See CB translation p. 1367 ff.

[**] See CB translation p. 1379 ff.

[***] See CB translation p. 429 ff, 435 ff.

TERTIARY ACETYLENIC ALCOHOLS

III. DEHYDRATION OF METHYL-n-PROPYLACETYLENYLCARBINOL AND OF α,α-ACETYLENYLCYCLOPENTANOL

I. A. Favorskaya and the Student L. V. Fedorova

One of the methods used to prepare hydrocarbons with conjugated double and triple bonds is the dehydration of tertiary acetylenic alcohols. Whenever the splitting out of the water can be done in two ways, the principal reaction product will be the isomer produced as the result of the detachment of a hydrogen atom from the least hydrogenated carbon atom. But no one has made a study – even an approximate one – of the proportions of the isomeric hydrocarbons produced by dehydrating tertiary acetylenic alcohols.

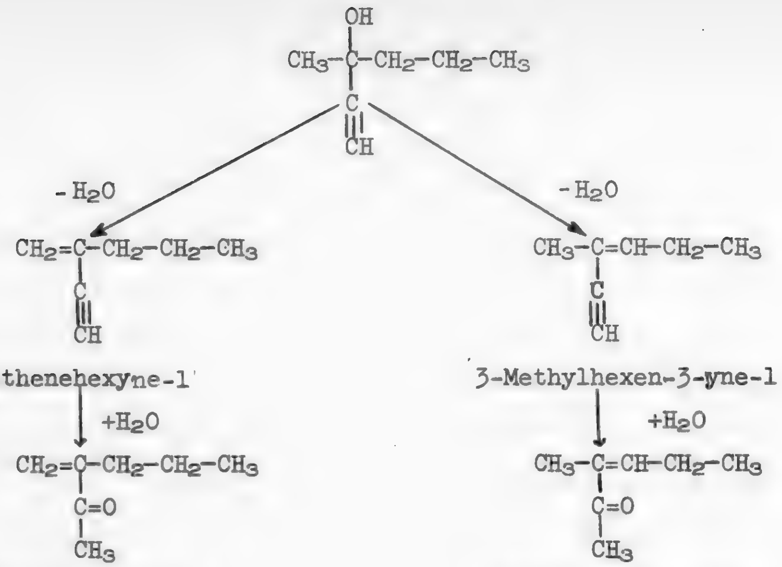
In the present paper we have endeavored to solve this problem for methyl-n-propylacetylenylcarbinol. Our interest in this investigation was stimulated by the following considerations: wholly pure individual hydrocarbons must be employed in studying the addition reactions of various agents to monovinylacetylenic hydrocarbons. But, if dehydration yields a mixture of two hydrocarbons, even narrow fractions collected in the coarse fractionation of the resultant mixture will not be individual hydrocarbons.

Shikhnev [1] made a study of the dehydration of methyl-n-propylacetylenylcarbinol over magnesium sulfate, investigating the 92-93° fraction, to which he assigned the structure of 3-methyl-3-hexenyne-1, on the basis of oxidation and ozonation. But in this case, we cannot judge the proportions in the mixture of isomeric hydrocarbons from their oxidation and ozonation; we can draw no conclusions as to the amount of butyric acid present when it exists in small amounts mixed with formic, acetic, and propionic acids.

We chose the following method of determining the percentages of isomeric hydrocarbons in the mixture: the mixture of hydrocarbons produced by dehydration was converted into the corresponding unsaturated ketones by the Kucherov method. The hydration products were fractionated in vacuum, semicarbazones prepared from the first and the last fractions, these semicarbazones proving to be semicarbazones of two different ketones. The amount of the ketone containing a terminal methylene group present in the intermediate fractions was determined by ozonation.

The problem involved the quantitative determination of formaldehyde and formic acid in the decomposition products of the ozonide. The method of quantitatively determining the terminal methylene group by ozonation was previously employed by D'Oeuvre [2] in determining the proportions of the α- and β- forms of methylheptanone. The author measured the quantity of the α-form, containing the terminal methylene group, by determining it in the ozonation products of the formaldehyde. The latter was determined colorimetrically, making use of the ability of formaldehyde to color a solution with a Gros-Bol reagent.

Inasmuch as the ozonide was decomposed with sulfur dioxide, it was believed that there is no formic acid among the decomposition products of the ozonide. In our investigation we employed the procedure worked out by A.I.Yakubchik [3] to determine the formaldehyde and the formic acid in the decomposition products of the ozonide.



3-Methenehexyne-1

3-Methylhexen-3-yne-1

3-Methenehexanone-2

3-Methylhexen-3-one-2 [12]

M.p. of the semicarbazone: 146-148°

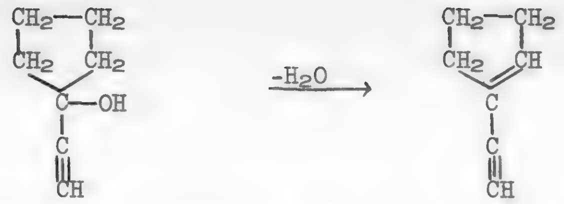
M.p. of the semicarbazone: 172°.

It is advisable to make a quantitative determination of the formic acid and of formaldehyde in the ozonation products of a mixture of isomers whenever only one of the isomers possesses a terminal methylene group. This method is particularly attractive whenever we are investigating a mixture of hydrocarbons, such as a mixture of an asymmetrical allene and a disubstituted acetylene that is isomeric with it. In our case, the quantitative data we secured may be regarded as merely approximate. First of all, in analyzing the mixture of ketones produced by hydrating the mixture of hydrocarbons, we assumed that both of the isomeric hydrocarbons, 3-methene-hexyne-1 and 3-methylhexen-3-yne-1 are hydrated with equal ease. There is no reference in the literature to the effect of substituents in the vinyl group of monovinylacetylene upon the ability of the triple bond to be hydrated. Moreover, the unsaturated ketones produced by hydration (by the Kucherov method) had to be purified via their semicarbazones, as the minutest contamination with a monovinylacetylenic hydrocarbon that had not been hydrated could spoil our determination; since the semicarbazones of the isomeric ketones possess different solubilities in alcohol, it is possible for us to change the composition of the mixture somewhat during this operation, lowering the percentage of the ketone with the terminal methylene group.

Our investigations have indicated that the ketone containing a terminal methylene group, 3-methenehexanone-2, totals about 30%.

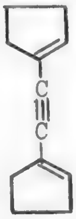
Therefore, our study of the products of the dehydration of methyl-n-propylacetylenylcarbinol has led us to conclude that a mixture of isomeric hydrocarbons is formed when water is split out of this carbinol.

We selected α,α-acetylenylcyclopentanol as a carbinol that yields a single product upon dehydration. We also chose this carbinol because the hydrocarbon produced during hydration will exist in only the cis form, since trans closure of a multiple bond is impossible in a five-membered ring. The resulting hydrocarbon, Δ_1-cyclopentenylacetylene, must be a completely individual hydrocarbon and must have a quite definite structural formula and a quite definite steric arrangement of its atoms.

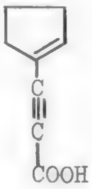


Determination of the molecular weight, the constant refractive index for all the fractions, and the molecular refraction all agree with this structure of the resultant hydrocarbon. Ultimate analysis yields results that conform to the formula C_7H_8. Oxidation of the hydrocarbon yields glutaric, succinic, and formic acids. The hydrocarbon forms a characteristic precipitate with ammoniacal cuprous chloride, providing a high yield of its sodium derivative and a 60% yield of Δ_1-cyclopentenylpropiolic acid. The hydrocarbon possesses still another interesting property, however, which does not follow from the formula suggested, and, it would appear, demonstrated, for it. This property is its intense yellow-green color, both in the liquid and in the gaseous state.

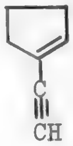
It is of interest to consider substances whose structure is analogous to that of the hydrocarbon we have secured:



White crystals [4]



White crystals



Yellow green liquid

We still cannot say why the hydrocarbon we have prepared, Δ_1-cyclopentenylacetylene, is an intense yellow green.

EXPERIMENTAL

Synthesis of methyl-n-propylacetylenylcarbinol [1,5,6]. We placed 150 g of powdered anhydrous KOH and 300 ml of absolute ether in a three-necked flask fitted with a propeller stirrer and a reflux condenser. The ether was saturated with acetylene at 0°, after which a solution of 75 g of methyl n-propyl ketone in 75 ml of absolute ether was added drop by drop to the reaction mixture during the course of 7 hours. A strong current of acetylene was passed through the reaction mixture throughout the experiment. The next day the resultant alcoholate was carefully decomposed with water, the alkaline solution was extracted with ether, and the ether solution was saturated with carbon dioxide and desiccated with potash. B.p. of methyl-n-propylacetylenylcarbinol: 135-137°; 63.7 g of carbinol prepared. Yield: 65%. A total of 8.7 g of glycol was secured as a by-product.

Dehydration of methyl-n-acetylenylcarbinol. 40 g of the carbinol was passed through a glass tube in an atmosphere of carbon dioxide, the tube being filled with unfired porcelain [7]. The dehydration temperature was 220-230°. The carbinol was passed through the tube for 7 hours. The reaction product was collected in a receiver chilled with ice; it separated sharply into two layers, the top one being the hydrocarbon, and the bottom one water. The hydrocarbon was desiccated above Na_2SO_4 and then distilled; distillation yielded the following fractions: 1) b.p. 85-90°, 2 g; 2) b.p. 91-94°, 14 g, n_D^{22} 1.4304; 3) b.p. 95-98°, n_D^{22} 1.4308, 3 g. The hydrocarbon yield averaged 50-55%. The hydrocarbon produces a characteristic yellow precipitate with ammoniacal cuprous chloride.

Hydration of the 85-98° hydrocarbon fraction. 26 g of the hydrocarbon mixture, 8.1 g HgO, 22 ml H_2SO_4, 500 ml H_2O in 64 ml of a 50% solution of ferric sulfate were placed in a flask fitted with a stirrer and a reflux condenser. The reaction mass was stirred vigorously and heated to 70° for 5 hours. The resulting ketones were distilled with steam, extracted with ether, and desiccated with $CaCl_2$. The ether was driven off, and the ketones were distilled in vacuum.

Fractions: 1) b.p. 35-38° at 14 mm, n_D^{21} 1.4260, 1.4 g; 2) b.p. 43-46° at 14 mm; n_D^{21} 1.4328, 4.3 g; 3) 47-52° at 14 mm, n_D^{21} 1.4390, 5 g; 4) b.p. 53-57° at 14 mm, n_D^{21} 1.4457, 1.6 g.

Fraction 1. The semicarbazone was prepared by taking 1.4 g of the fraction with a b.p. of 35-43° at 14 mm dissolved in 1.5 ml of alcohol, 3 g of semicarbazide hydrochloride, 3 g of CH_3COOK, 4.5 ml H_2O, and 3 ml of alcohol. This yielded 1.1 g of the semicarbazone (52.4% of the theoretical). The resultant semcarbazone is very soluble in alcohol. The semicarbazone had a melting point of 146-148° after recrystallization from aqueous alcohol.

0.0704 g substance: 15.3 ml N_2 (18°, 760 mm). 0.0800 g substance: 17.2 ml N_2 (18°, 760 mm). Found %: N 25.00, 24.75. $C_8H_{15}ON_3$. Computed %: N 24.85.

Fraction 4. 1.6 g of the ketone (b.p. 53-57° at 14 mm) yielded 2.4 g of the semicarbazone (100%). The semicarbazone is sparingly soluble in alcohol and in benzene. It fuses at 172° after recrystallization from alcohol.

0.0645 g substance: 13.9 ml N_2 (17°, 758 mm). 0.0623 g substance: 13.3 ml N_2 (18°, 760 mm). Found %: N 25.0, 24.85. $C_8H_{15}ON_3$. Computed %: N 24.85.

A test sample of the semicarbazone with a m.p. of 146-148°, mixed with the semicarbazone with a m.p. of 172° fused at 140-156°. These figures indicate that these are two different semicarbazones, representing different ketones.

We made a quantitative determination of the amount of ketone with a terminal methylene group in the second and third fractions of the ketone mixture, with a b.p. of 43-52° at 14 mm. Analysis of Fractions 2 and 3 indicated that they contain a minute trace of the hydrocarbon. Fraction 2 produces an insignificant yellowish turbidity with ammoniacal cuprous chloride, while Fraction 3 yields no precipitate of copper acetylenide, though ultimate analysis of this fraction indicates a somewhat higher percentage of carbon (some 1.5%), evidence of the trace of the hydrocarbon. The traces of the hydrocarbon were eliminated from the ketone mixture by converting the latter into semicarbazones and then regenerating the ketones from the latter. The ketone mixture then boiled at 30-41° at 7 mm.

Ozonation of the ketone mixture with a b.p. of 30-41° at 7 mm. 4 g of the ketone mixture was dissolved in 40 ml of chloroform. Ozonation was effected by the A.I.Yakubchik method, allowing for the concentration of ozone before and after the test tube containing the substance was weighed.

4 g of the ketone theoretically required 1.71 g of O_3, but it actually absorbed 1.97 g of O_3. Ozonation was stopped when the concentration of ozone behind the test tube containing the substance became constant. The ozonides were decomposed by heating them with 70 ml of water over a water bath.

The formaldehyde was determined quantitatively by condensation with dimedone. 5 ml of the ozonide solution was added to 0.2 g of dimedone dissolved in 100 ml of boiling water. When the mixture boiled, 0.0488 g of a precipitate was thrown down. M.p. 187-189°. A test sample fused at 188-189° when mixed with the known condensation product of formaldehyde and dimedone. The formaldehyde totaled 0.09 g, recomputed in terms of the entire solution. The formic acid was determined quantitatively by the Finke method [8]. The formic acid found in the ozonide decomposition products totaled 0.3319 g, equivalent to 0.2164 g of formaldehyde. The total formaldehyde, i.e., that determined by the Finke method plus the free formaldehyde determined via dimedons, was 0.368 g. Hence the 3-methene hexanone-2 ketone totaled 1.37 g. The quantity of ketones in Fractions 1 and 2 was recomputed from the total semicarbazones. The overall quantity of 3-methene-hexanone-2 totaled 2.06 g. Hence, the mixture contained about 30% of the ketone with a terminal methylene group.

Synthesis of α,α-acetylenylcyclopentanol [4]. The α,α-acetylenylcyclopentanol was synthesized by the well-known A.E.Favorsky reaction. 150 g of powdered anhydrous KOH and 400 ml of absolute ether were placed in a three-necked flask. After the ether had been saturated with acetylene, 50 g of the ketone dissolved in 350 ml of ether was added in the course of 10 hours. The carbinol yield was 60.3 g, or 92% of the theoretical. 3 g of glycol was recovered as a by-product. The boiling point of the carbinol was 159-161°. The distilled carbinol solidified into acicular crystals with a m.p. of 26-28°.

Dehydration of α,α-acetylenylcyclopentanol. 80 g of the carbinol was passed through a glass tube filled with unfired porcelain for 9 hours in an atmosphere of carbon dioxide. The dehydration temperature was 240-250°. The reaction product was collected in a receiver chilled with snow. The crude product weighed 70.7 g. The resultant product was distilled into a tower in vacuum.

Fractions: 1) b.p. 56-59° at 100 mm, n_D^{20} 1.4875, 8.4 g; 2) b.p. 60-61° at 100 mm, n_D^{20} 1.4880, 9.8 g; 3) residue (did not distil) – the carbinol.

The yield of the hydrocarbon was 30-40% of the theoretical. Immediately after its preparation the hydrocarbon is a highly mobile volatile liquid, gradually turning viscous upon standing; it forms a characteristic precipitate with ammoniacal cuprous chloride, and forms a precipitate with ammoniacal silver nitrate. An extremely interesting peculiarity of this hydrocarbon is its intensely yellow-green color, which is visible even in its vapor.

B.p. 60-61° at 100 mm; d_4^{20} 0.8587; n_D^{20} 1.4880; MR_D 30.87; computed 29.86.

0.1067 g substance: 0.3568 g CO_2; 0.0883 g H_2O. 0.1130 g substance: 0.3779 g CO_2; 0.0930 g H_2O 0.1787 g substance: 16.73 g benzene: Δt 0.61°; 0.2740 g substance: 16.73 g benzene: Δt 0.88°. Found %: C 91.19, 91.21; H 9.24, 9.12; M 90.7, 96.4. C_7H_8. Computed %: C 91.24; H 8.76; M 92.

Ozonation of the hydrocarbon yielded an exceptionally stable ozonide, which turned into tar when decomposed.

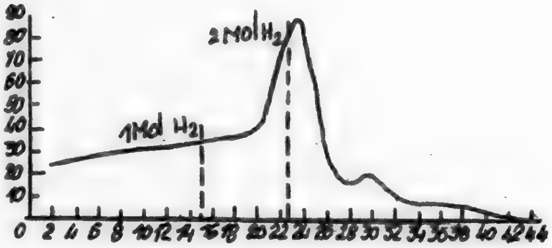
0.4 g of the hydrocarbon and 320 ml of acetone were used for oxidation. Oxidation was effected with a 3% permanganate solution (56 g of $KMnO_4$ in 1800 ml of H_2O). Oxidation yielded minute amounts of two acids: 1) an acid with a m.p. of 94-95°, a test sample of which fused at 94-95° when mixed with known glutaric acid; and 2) an acid with a m.p. of 177-179°, a test sample of which fused at 180-181° when mixed with known succinic acid. Considerable formic acid was also found in the oxidation products.

Hydrogenation of Δ_1-cyclopentenylacetylene. The Δ_1-cyclopentenylacetylene was hydrogenated catalytically with Pt black in a solution of ethyl alcohol. 0.8 g of the hydrocarbon in 50 ml of alcohol and 0.1 g of platinum black were used. Theoretically, 584 ml of H_2 is required. Actually 570 ml of H_2 (0°, 760 mm) was absorbed, i.e., 97.6% of the theoretical (cf. the table).

The shape of the resultant curve (cf. the figure) is typical of acetylenic hydrocarbons [9]. The resultant solution of the hydrogenated substance is colorless; it forms no precipitate with ammoniacal silver nitrate; and it does not decolorize a permanganate solution.

Time, minutes	H_2 absorbed, ml	Time, minutes,	H_2 absorbed, ml	Time, minutes	H_2 absorbed, ml
2	23	2	74	2	1.6
2	23	2	88.6	2	1.0
2	28.4	2	30.8	2	0.6
2	28.8	2	16.8	4	0.8
2	30.5	2	21.2	4	0.8
2	30.8	2	10.6	4	0.8
2	32.3	2	7.4	6	0.4
2	36.4	2	6.4	10	0.3
2	36.8	2	4	25	0.5
2	39.7			45	1.2

Preparation of Δ_1-cyclopentylpropiolic acid. 1.2 g of metallic sodium was heated to boiling in absolute xylene. After the sodium melted, the sodium was converted into finely divided metal by rapidly and vigorously shaking the flask containing the molten sodium. 4 g of Δ_1-cyclopentenylacetylene was added to the cooled sodium in the xylene. At the beginning, the mixture had to be heated to 90° for the reaction to set in, after which the temperature rose by itself to 110°. The whole reaction flask was filled with a precipitate of the sodium derivative. After the mixture had cooled, anhydrous carbon dioxide was passed through it for 20 hours. The resulting salt was extracted with water, and the acid was extracted with ether after acidulation with dilute H_2SO_4. The ether solution was desiccated above calcined Na_2SO_4. The ether was driven off in vacuum, the acid remaining in the flask as a crystalline mass. The yield of crude acid was about 60% of the theoretical. The acid fused at 139-140° after recrystallization from benzene.



0.1148 g substance: 0.2991 g CO_2; 0.0586 g H_2O. 0.1096 g substance: 18.23 g glacial acetic acid: Δt 0.18°. 0.0392 g substance: consumed 2.9 ml 0.1 N NaOH; 0.1136 g substance: consumed 8.3 ml 0.1 N NaOH. Found %: C 71.05; H 5.71; M 137.2; equiv. 137.3, 137.3. $C_8H_8O_2$. Computed %: C 70.58; H 5.92; M 136; equiv. 136.

An excess of silver nitrate solution was added to the solution of the sodium salt. The precipitated silver salt was filtered out and washed with a small amount of water.

0.1064 g substance: 0.0556 g Ag. 0.1167 g substance: 0.0620 g Ag. Found %: Ag 52.20, 53.1. $C_8H_7O_2Ag$. Computed %: Ag 44.44. $C_8H_7O_2Ag \cdot AgNO_3$. Computed %: Ag 52.30.

The formation of a double salt is due to the presence of conjugated double and triple bonds in the acid; one of the present authors [10] has observed a similar phenomenon in the case of β-tert-butylmonovinylacetylenecarboxylic acid; on the other hand, A.E.Favorsky [11] has pointed out that the silver salts of acetylenecarboxylic acids decompose into carbon dioxide and a silver derivative of the hydrocarbon. It is possible that this phenomenon, i.e., the partial decomposition of the salt, is also responsible for the slightly increased percentage of silver in the second analysis. We obtained further proof that double silver salts are formed only by acids that contain conjugated double and triple bonds by hydrogenating an aqueous solution of the sodium salt of Δ_1-cyclopentenylpropiolic acid above spongy palladium. Analysis of the silver salts in the hydrogenation products showed that the composition of the salts was close to the normal one.

SUMMARY

1. Dehydration of methyl-n-propylacetylenylcarbinol above unfired porcelain at 220-230° results in the formation of a mixture of the isomeric hydrocarbons 3-methenehexyne-1 and 3-methylhexen-3-yne-1.

2. Hydrating the mixture of hydrocarbons yielded a mixture of the unsaturated ketones 3-methylhexanone-2 and 3-methylhexen-3-one-2. The ketones were identified as their semicarbazones.

3. The hydrocarbon Δ_1-cyclopentenylacetylene was prepared by dehydrating α,α-acetylenylcyclopentanol above unfired porcelain.

4. Δ_1-cyclopentenylpropiolic acid was prepared via the sodium derivative of the hydrocarbon.

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Chair of the Structure of Organic
Compounds
Leningrad State University

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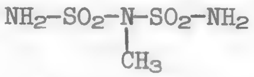
*See CB translation p. a-521 ff.

THE METHYLATION OF IMIDOSULFAMIDE

A. V. Kirsanov and Yu. M. Zolotov

Not a single alkyl imidosulfamide is known up to the present time. It was the objective of the present research to produce and study the properties of 3-monomethylimidosulfamide. Two methods were used to synthesize 3-monomethylimidosulfamide, viz.: reacting methyl iodide with the silver salt of imidosulfamide, and reacting diazomethane with free imidosulfamide. It was found that methyl iodide reacts fairly rapidly with the silver salt of imidosulfamide at room temperature, only one molecule of the methyl iodide entering into reaction with one molecule of the silver salt during the course of 24 hours, after which the reaction comes to a stop. The reaction products included: some 25.9% of the theoretical amount of crystalline monomethylimidosulfamide, some 36.5% of the theoretical amount of free imidosulfamide, and some 14% of noncrystallizing oily products, probably polymethylimidosulfamides, which have not been investigated in any detail so far. The reaction products were separated by treatment with various solvents, followed by crystallization. An endeavor was made to separate the free imidosulfamide from the methylated forms by reacting it with ammonia in ether solution, inasmuch as methylimidosulfamide possesses no acid properties, while imidosulfamide is a strong monobasic acid.* We had to abandon this procedure, however, since tests run with the pure substances showed that methylimidosulfamide forms a crystalline double compound with ammonia in ether solution, the curious properties of which will will be reported on in one of our forthcoming papers. The same methylimidosulfamide was secured with a much better yield, some 75% of the theoretical, by reacting diazomethane with free imidosulfamide in absolute ether. The first molecule of diazomethane reacts with the imidosulfamide nearly instantaneously, though subsequent methylation is much slower.

3-Methylimidosulfamide is a colorless crystalline substance with a m.p. of 113-114°, which dissolves readily in water, exhibiting a neutral reaction. The neutral reaction of a freshly prepared aqueous solution proves that the methyl is attached to the middle nitrogen atom, i.e., that this methylimidosulfamide has the structure of 3-methylimidosulfamide:



$$NH_2{-}SO_2{-}\underset{\displaystyle CH_3}{\underset{|}{N}}{-}SO_2{-}NH_2$$

3-Methylimidosulfamide is very easily hydrolyzed: at room temperature, its aqueous solutions exhibit an acid reaction with dimethylyellow within 15 minutes of their preparation. Hydrolysis is apparently instantaneous when the solution is boiled, apparently as follows:

$$NH_2{-}SO_2N(CH_3){-}SO_2{-}NH_2 \xrightarrow[+H_2O]{} NH_2{-}SO_2{-}NHCH_3 + NH_2SO_2OH.$$

Hence, the hydrolysis products must include the hitherto unknown monomethylsulfamide.

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*A. V. Kirsanov and Yu. M. Zolotov, J. Gen. Chem. 20, 1790 (1950); see CB translation p. 1851 ff.

EXPERIMENTAL

Methylation of the silver salt of imidosulfamide with methyl iodide. After a few preliminary tests employing data on the solubilities of the pure substances, the following were found to be the optimum conditions for methylation and separation of the reaction products. 0.01 mole of the silver salt of imidosulfamide (2.82 g), carefully dried in vacuum and carefully pulverized, was mixed with 2.0 ml of methyl iodide, after which the reaction mixture was set aside to stand in the dark. The next day, the excess methyl iodide was driven off in vacuum. The residue weighed 3.26 g, i.e., its gain in weight totaled 1.44 g instead of the 1.42 g called for. The dry product was treated for 1 hour with 100 ml of absolute ether, the ether solution was filtered, and the residue was extracted three more times, using 15 ml of ether each time. The combined ether extracts were evaporated to dryness, first over a water bath at atmospheric pressure and then in vacuum. After about half of the volume of ether had been driven off, a crystalline precipitate began to settle out, the amount of the precipitate increasing as evaporation progressed. The dry residue weighed 1.62 g; the substance was readily soluble in water, exhibiting a strong acid reaction. To remove the bulk of the free imidosulfamide, which was much less soluble in ether than the methylimidosulfamide, the dry residue was treated for an hour with 50 ml of absolute ether, the insoluble residue then being filtered out, washed three times with 1 ml of ether, and dried in a vacuum desiccator. This yielded 0.41 g of free imidosulfamide with a m.p. of 162-163°; a test sample fused at 163-164° when mixed with known imidosulfamide. Recrystallization from 2 ml of acetone and 6 ml of benzene yielded 0.3 g of snow-white needles, with a m.p. of 164-165°, a mixed test sample fusing at the same temperature. The ether solution was evaporated to dryness, at first over a water bath at atmospheric pressure, and then in vacuum. The residue totaled 1.12 g of a colorless crystalline product which softened at about 90° and fused at about 110°. The monomethylimidosulfamide was recovered by boiling the product for 30 minutes with 150 ml of absolute benzene, filtering the benzene extract while boiling, and again extracting the residue with 150 ml of boiling benzene. When the first benzene extract cooled, 0.25 g of light, snow-white flat needles, with a m.p. of 113-114° settled out, the second extract yielding 0.15 g with a m.p. of 114-115°. Evaporation of the benzene mother liquor to a volume of 75 ml caused another 0.09 g of the same product to settle out. Thus, the total yield of methylimidosulfamide was 0.49 g, or about 25.9% of the theoretical.

The 0.25 g of residue that did not dissolve in benzene represented contaminated imidosulfamide. The product was purified by dissolving it in 10 ml of ethyl acetate, the slight deposit being filtered out of the solution, and the latter being evaporated to dryness in vacuum. The residue contained 0.23 g of imidosulfamide with a m.p. of 154-158°; a mixed test sample fusing at 156-160°; snow-white needles with a m.p. of 162-163° after recrystallization from acetone and benzene. Hence, the total yield of free imidosulfamide was 0.64 g, or 36.5% of the theoretical.

The benzene mother liquors of the methylimidosulfamide were evaporated to dryness, in vacuum toward the end of the process. The residue was 0.28 g of an oily noncrystalline liquid, which probably was a mixture of a small amount of monomethylimidosulfamide and dimethylimidosulfamide or higher polymethyl derivatives. The yield of this product was about 14% of the theoretical, based on the dimethyl derivative; hence, the overall yield of all three reaction products was about 76.4% of the theoretical.

Methylation of free imidosulfamide with diazomethane. 0.03 mol of pulverized imidosulfamide (5.25 g) was mixed with 100 ml of absolute ether; the mixture was chilled to 10°, and a solution of diazomethane in ether, containing 0.03 mol of diazomethane (87 ml of a 0.345 N solution), was added to the mixture, with vigorous manual stirring. Nitrogen was evolved violently, the solution was decolorized, and nearly all the precipitate dissolved. Any lumps that formed were broken up with a glass muddler. Another 5 ml of this solution of diazomethane was added, and it took 15 seconds for the solution to be decolorized; when another 5 ml was added, the yellow color persisted for minutes.[*]

A small quantity of activated charcoal was added to the slightly turbid ether solution, which was then filtered, yielding a transparent, colorless ether solution, which was evaporated over a water bath to an aggregate weight of 50.0 g, crystals beginning to form from the hot solution. 250 ml of absolute benzene was added during the course of 1 or 2 minutes to the hot solution, while the latter was slowly stirred by hand, and the whole was set aside for 2 hours to crystallize. The methylimidosulfamide settled out of the solution as fine, colorless, transparent, highly refractive, flat prisms, which were extremely hard and stuck to the walls and bottom of the flask with unusual tenacity. Suction filtering, washing with benzene, and drying in a vacuum desiccator yielded 3.7 g of methylimidosulfamide with a m.p. of 113-114°. The ether was driven off from the mother liquor, together with part of the benzene, until its weight totaled 180 g, and the slightly turbid solution was set aside to stand overnight. This caused light flat needles to settled out; they were suction-filtered, washed with benzene, and recrystallized from 5 ml of acetone, followed by precipitation with 25 ml of benzene. Within 2 hours large beautifully formed, transparent, water-white prisms settled out; they were suction filtered 12 hours later, washed with benzene, and desiccated in vacuum. This yielded another 0.6 g of methylimidosulfamide with a m.p. of 112-113°. The aggregate yield of monomethylimidosulfamide totaled 4.3 g, or 75.7% of the theoretical. All the mother liquors were combined and evaporated to dryness, in vacuum toward the end of the process. The residue was 0.43 g of a light-yellow oily liquid, which slowly yielded a small quantity of two kinds of crystals, prisms and needles. The bulk of this product probably consisted of polymethylimidosulfamides, which were not investigated in detail.

The entirely pure monomethylimidosulfamide fuses at 114-115° (uncorr.), though it begins to sweat at 112°. Methylimidosulfamide has a slightly bitter taste; its freshly prepared aqueous solutions are also slightly bitter, but their taste quickly turns intensely sour when allowed to stand at room temperature.

Methylimidosulfamide is highly soluble in water, methanol, ethyl alcohol, acetone, and ethyl acetate, but it is very slightly soluble in carbon tetrachloride, slightly soluble in cold benzene, and somewhat more soluble in hot benzene. It is easy to crystallize small amounts of methylimidosulfamide from boiling benzene. When 100 g of a saturated boiling solution is cooled to 20 g, 0.22 g of the substance settles out as flat, light, snow-white needles that are nearly invisible when in the liquid. At 20° only 0.033% of methylimidosulfamide is soluble in benzene (149.1 g of saturated solution contains 0.0490 g of the substance). It is easier to crystallize large quantities of methylimidosulfamide by precipitating it with benzene from an ether solution as described above, or, even better, by precipitating it with five volumes of benzene from an acetone or ethyl acetate solution, the methylimidosulfamide then settling out as transparent, flat, lustrous prisms. At 20°, a saturated acetone solution contains less that 49.3% and more than 46.9% of methylimidosulfamide (0.77 g of the substance did not dissolve completely in 0.79 g of acetone, but did dissolve in 0.87 g of acetone). At 18° a saturated ether solution contains 2.86% of methylimidosulfamide, 100 ml containing 2.04 g (6.17 g of the saturated solution contained 0.1762 g of the substance).

0.5013 g substance: 0.1192 g CO_2; 0.1688 g H_2O. 0.5267 g substance:

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[*] The addition of a large excess of diazomethane should be avoided, since this reduces the yield of methylimidosulfamide and increases the yield of the noncrystallizing products.

0.1228 g CO_2; 0.1742 g H_2O. 7.23 mg substance: 1.393 ml N_2 (19°, 756 mm). 6.34 mg substance: 1.227 ml N_2 (19°, 756 mm). 0.1113 g substance: 0.2733 g $BaSO_4$. 0.1217 g substance: 0.2991 g $BaSO_4$. 0.6375 g substance: in 10 ml water: 6.7 ml 0.5 N alkali (titration of the hot solution with phenolphthalein). Found %: C 6.37, 6.36; H 3.70, 3.70; N 22.41, 22.51; S 33.73, 33.75; M 190.3. $CH_7O_4N_3S_2$. Computed %: C 6.34; H 3.73; N 22.21; S 33.88; M 189.2.

SUMMARY

3-Monomethylimidosulfamide has been synthesized and its properties described.

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THE PHOTOREACTION OF PHENYLMERCURY HYDROXIDE

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Previously published papers [1] have described the photoreaction of organometallic compounds of mercury of the R_2Hg type. It has been the objective of the present research to investigate the analogous reactions for mixed mercury derivatives, RHgX. Halogen compounds, RHgHal, have been frequently synthesized in the photoreactions of R_2Hg in solvents containing halogens, manifesting themselves as very unreactive substances. They undergo no appreciable change upon prolonged irradiation. We therefore took as the substances for investigation phenylmercury hydroxide and phenylmercury acetate. Both of these substances react ionically in many reactions, dissociating as follows:

$$C_6H_5HgOH \rightleftarrows C_6H_5Hg^{\cdot} + HO'.$$

It might have been thought, however, that the action of light in solvents with a low dielectric constant would cause the reaction to yield the following radicals:

$$C_6H_5 : Hg : OH \xrightarrow{h\nu} C_6H_5 : Hg\cdot + \cdot OH.$$

Experimental data have borne out this supposition. Phenylmercury acetate reacted with great difficulty, a photoreaction taking place only in a solution of cellosolve. Phenylmercury hydroxide reacted readily, however, so that most of our investigations were made with that compound. We tested carbon tetrachloride, chloroform, methanol, cellosolve, benzene, toluene, chlorobenzene, and nitrobenzene. The nature of the photoreactions generally resemble those of diphenylmercury, though they exhibit several singularities.

In every case the hydroxyl radical detaches hydrogen from the solvent, turning into water. When the reaction is carried out in carbon tetrachloride, water is also formed, but here the hydrogen is detached from the C_6H_5Hg radical, which is transformed into an insoluble organomercury compound, which was not investigated any further. The C_6H_5Hg radical formed during photolysis reacts with solvents exactly as in the photoreactions of diphenylmercury, which forms a similar radical when acted upon by light. Phenylmercury chloride is formed in solvents that contain halogen (CCl_4, $CHCl_3$). The process takes place as follows in these solvents, on the whole.

Chloroform:

$$C_6H_5HgOH + h\underline{v} \longrightarrow C_6H_5Hg\cdot + \cdot OH.$$

$$CHCl_3 + \cdot OH \longrightarrow H_2O + \cdot CCl_3.$$

$$C_6H_5Hg\cdot + CHCl_3 \longrightarrow C_6H_5HgCl + \cdot CHCl_2 \text{ (principal reaction).}$$

$$\left\{\begin{array}{l} C_6H_5Hg \longrightarrow C_6H_5\cdot + Hg \\ C_6H_5\cdot + CHCl_3 \longrightarrow C_6H_6 + \cdot CCl_3 \end{array}\right. \quad \text{(side reactions)}$$

$$2\cdot CCl_3 \longrightarrow C_2Cl_6.$$

The metallic mercury formed at first reacts with the chloroform later, under the action of light, yielding calomel and corrosive sublimate.

Carbon tetrachloride:

$$C_6H_5HgOH + h\underline{v} \longrightarrow C_6H_5Hg^{\cdot} + {}^{\cdot}OH.$$

$$C_6H_5Hg^{\cdot} + {}^{\cdot}OH \longrightarrow H_2O + (C_6H_4Hg) \text{ etc.}$$

$$C_6H_5Hg^{\cdot} + CCl_4 \longrightarrow C_6H_5HgCl + {}^{\cdot}CCl_3.$$

$$2{}^{\cdot}CCl_3 \longrightarrow C_2Cl_6$$

Thus only some of the C_6H_5Hg radicals form phenylmercurychloride; the others are lost as the result of their yielding up hydrogen to the hydroxyl groups.

When dissolved in methanol or cellosolve, the C_6H_5Hg radical breaks down into mercury and the phenyl radical, which is converted into benzene and an aldehyde as the result of detachment of hydrogen from the solvent. The equations for these reactions are:

$$C_6H_5HgOH + CH_3OH \xrightarrow{hv} C_6H_6 + Hg + H_2O + CH_2O.$$

$$C_6H_5HgOH + C_2H_5OCH_2CH_2OH \longrightarrow C_6H_6 + Hg + H_2O + 2CH_3CHO.$$

Side reactions result in the formation of a slight amount of diphenyl via dimerization of the phenyl radical. The reaction proceeds with much more difficulty in a benzene solution. Diphenyl, water, and mercury are recovered after irradiation. Hence, the equation involved is:

$$C_6H_5HgOH + C_6H_6 \longrightarrow C_6H_5{-}C_6H_5 + Hg + H_2O.$$

This reaction is quite analogous to the decomposition of phenyldiazonium hydroxide in benzene [2]:

$$C_6H_5N_2OH + C_6H_6 \longrightarrow C_6H_5{-}C_6H_5 + N_2 + H_2O;$$

hence, we have here an amphoteric substitution reaction, as is common in many processes, such as diazonium salts, peroxides, nitroso acyl aryl amines, etc., [3].

To check this assumption we had to use some other aromatic solvent, instead of benzene. Then diphenyl ought to be substituted in accordance with the following reaction:

$$C_6H_5HgOH + ArH \longrightarrow C_6H_5Ar + Hg + H_2O.$$

Tests made with nitrobenzene and chlorobenzene did not yield positive results. Comparatively little mercury was evolved, a complex mixture of products being recovered and the reaction being accompanied by considerable tarring. Part of the chlorine was detached from the chlorobenzene by the mercury. The results were good in the toluene solution, the photoreaction taking place as expected:

$$C_6H_5HgOH + C_6H_5CH_3 \longrightarrow C_6H_5C_6H_4CH_3 + Hg + H_2O.$$

Besides this main reaction, we also observed the formation of benzene as the result of the detachment of hydrogen from the solvent by the phenyl radical.

$$C_6H_5HgOCOCH_3 + C_2H_5OCH_2CH_2OH \xrightarrow{hv} C_6H_6 + Hg + CH_3COOH + 2CH_3CHO.$$

A small amount of diphenyl is formed as a by-product.

EXPERIMENTAL

The experiments were performed in quartz test tubes, which were hermetically sealed by stoppers. When solvents that were insoluble in water were used, a glass cup was affixed to the stopper, containing calcined copper sulfate to absorb the water evolved during the reaction. Irradiation was provided by a PRK-2 mercury quartz lamp.

Reaction of C_6H_5HgOH with methanol in cellosolve. The mercury evolved was separated from the solution after the reaction, washed, dried, and determined gravimetrically. The solution was distilled, the initial fractions being diluted with water; this caused benzene to separate out. The amount of benzene was determined gravimetrically. The benzene was identified by nitrating it to m-dinitrobenzene and finding its melting point, as well as that of a test sample mixed with the pure dinitrobenzene. No depression was observed. The aqueous layer left after the removal of the benzene contained aldehydes, their presence being demonstrated by means of the usual reactions.

The formaldehyde formed in the test with methanol was isolated as 1.2 g of a dimedone derivative with a m.p. of 189°, representing 0.06 g of formaldehyde. The residue left after the solvent had been removed was distilled with steam; this yielded diphenyl, with a m.p. of 70°, which exhibited no depression when mixed with the pure substance. The test results are listed in Table 1.

TABLE 1

Used			Irradiation time, hours	Recovered					
C_6H_5HgOH	Solvent			Mercury		Benzene		Diphenyl	
	Name	(ml)		g	%	g	%	g	%
2.82	Cellosolve	25	15	1.78	94	0.60	71	0.04	3
2.06	Methanol	25	20	1.15	82	0.32	59	0.01	4

Reaction of C_6H_5HgOH with chloroform and carbon tetrachloride. The precipitate that formed was filtered out after the reaction. The corrosive sublimate was washed out with hot water. Phenylmercury chloride was extracted from the residue with hot acetone. Its melting point was 251° after recrystallization, exhibiting no depression with the pure substance. The residue left behind after the acetone extraction (in the chloroform test) contained calomel and mercury, the carbon tetrachloride residue containing an insoluble organomercury compound which was not investigated any further. The solvent was driven off from the filtrate. The chloroform distillate was nitrated, yielding m-dinitrobenzene, with a m.p. of 89°. The residue left after the solvent had been driven off was steam distilled, yielding hexachloroethane, which fused at 183° in a sealed capillary after purification (Table 2).

TABLE 2

Used			Irradiation time, hours	Recovered												
C_6H_5HgOH	Solvent			C_6H_5HgCl		$HgCl_2$		Hg_2Cl_2		Hg		C_6H_6		H_2O		C_2Cl_6
	Name	ml		g	%	g	%	g	%	g	%	g	%	g	%	g
2.15	$CHCl_3$	25	40	0.97	41	0.12	6	0.65	34	0.10	7	0.05	8	0.11	95	0.16
1.70	CCl_4	20	40	1.10	67	–	–	–	–	–	–	–	–	0.07	71	0.10

Reaction of C_6H_5HgOH with benzene. 1.85 g of phenylmercury hydroxide was irradiated in 25 ml of benzene for 90 hours. The water evolved totaled 0.07 g, according to the gain in weight of the copper sulfate, or 57% of the theoretical. The mercury evolved was separated from the solution; it totaled 0.70 g, or 55% of the theoretical. The benzene was driven off, and the residue was distilled with steam. This yielded 0.18 g of diphenyl with a m.p. of 70°, which exhibited no depression with the pure substance. The diphenyl yield was 21%.

Reaction of C_6H_5HgOH with toluene. 3.32 g of phenylmercury hydroxide was irradiated in 40 ml of toluene for 60 hours. The copper sulfate gained 0.16 g in weight, representing an evolution of water that was 82% of the theoretical. The mercury was separated from the solution; it weighed 1.8 g (80% of the theoretical). The solvent was driven off. The first fraction, totaling 1 ml, was oxidized with potassium permanganate. Oxidation of the toluene left benzene, which was converted into m-dinitrobenzene, with a m.p. of 89°, exhibiting no depression with the pure substance, by nitration. This yielded 0.08 g of dinitrobenzene, equivalent to a benzene yield of 4%. The residue left after the solvent had been driven off was distilled in vacuum, 1.5 g of the fraction boiling at about 112° at 20 mm being collected. The analysis and properties of the substance recovered indicated that it was a mixture of the ortho and para isomers of methyldiphenyl.

0.1893 g substance: 0.6323 g CO_2; 0.1325 g H_2O. Found %: C 91.1; H 7.66. $C_{13}H_{12}$. Computed %: C 92.80; H 7.20. Substance: 0.1350, 0.2002, 0.2554 g; benzene 11.345 g: Δt 0.347, 0.544, 0.684°. Found: M 171.3, 163.1, 165.2. Computed M 168.1. The methyldiphenyl was oxidized to diphenylcarboxylic acid. The latter was titrated back in an alcoholic solution with phenolphthalein to determine the equivalent.

7.4 mg substance: 2.2 mg KOH, representing 105% in terms of $C_6H_5C_6H_4COOH$.

$C_6H_5HgOCOCH_3$ with cellosolve. 2.85 g of phenylmercury acetate was irradiated for 30 hours in 25 mg of cellosolve. The mercury evolved was separated from the solution. The mercury totaled 1.6 g, or 98% of the theoretical. The solvent was driven off. The first 5 ml of distillate was distilled with water, yielding 0.5 g of benzene (82% of the theoretical); the benzene was identified as m-dinitrobenzene. The aqueous solution had an acid reaction, and it was proved to contain acetic acid (qualitative reaction and analysis of the silver salt). The residue left after the solvent had been driven off was distilled with steam. This yielded traces of diphenyl. Acetaldehyde was found in the absorber that had been connected to the reaction tube during the test. The aldehyde was identified as the 2,4-dinitrophenylhydrazone, with a m.p. of 165°.

SUMMARY

1. A study has been made of the photoreactions of phenylmercury hydroxide with chloroform, carbon tetrachloride, methanol, cellosolve, benzene, and toluene.

2. Equations for reactions involved are set forth, on the assumption of a primary dissociation of the hydroxide into radicals.

3. The resulting radicals react, depending upon the solvent, detaching hydrogen from the solvent and forming benzene and water. The $C_6H_5Hg\cdot$ radical forms phenylmercury chloride in the solvents that contain a halogen. An amphoteric substitution reaction takes place in the benzene and toluene solutions.

4. The photoreaction of phenylmercury acetate in cellosolve is similar, yielding benzene, mercury, acetic acid, and acetaldehyde.

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THE PHOTOREACTIONS OF ORGANOMETALLIC COMPOUNDS OF MERCURY IN SOLUTION

VI. THE REACTIONS OF DIMESITYLMERCURY

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In our previously published papers [1] we investigated the reactions of diaryl mercury with various organic solvents under the action of ultraviolet light. A set of reactions was suggested, the first stage of which was the dissociation of the organomercury compound into radicals. Using the photoreactions of organometallic compounds, we are thus able to investigate the behavior of various radicals. Up to the present time tests have been made with phenyl, o-toluene, benzyl, and naphthyl derivatives of mercury.

The behavior of the o-toluene radical proved to be very much like that of the phenyl radical. Introducing a single methyl group into the benzene ring makes very little difference in the properties of the radical. We were intrested in making a study of dimesitylmercury. The inductive effect of three methyl groups increases the electron density of the benzene ring, which ought to be manifested in a weakening of the bond between that ring and the mercury atom, thus distinguishing the mesityl radical from the others.

The dimesityl mercury was prepared from bromomesitylene and sodium amalgam, the yield totaling 21.3%. Michaelis [2] had previously synthesized dimesitylmercury with very low yields, according to the author himself. He did not specify the synthesis conditions. Irradiating dimesitylmercury with ultraviolet light in a cellosolve or isopropyl alcohol solution causes it to break down like diphenylmercury, yielding metallic Hg and mesitylene as follows:

$$Mes_2Hg + C_2H_5OCH_2CH_2OH \longrightarrow 2MesH + Hg + CH_3C\begin{smallmatrix}\nearrow O\\ \searrow H\end{smallmatrix}$$

$$Mes_2Hg + CH_3CHOHCH_3 \longrightarrow 2MesH + Hg + CH_3COCH_3$$

(Mes = mesityl)

The reaction of dimesitylmercury in chloroform or in CCl_4 was somewhat different from that of diphenylmercury. In its photoreaction, one radical was detached, forming phenylmercurychloride. Both radicals are detached from the dimesitylmercury under analogous conditions. No mesitylmercury chloride was found in the reaction products. The mesityl radical reacted with the solvent as did the phenyl radical, i.e., it detached a hydrogen atom from chloroform, forming mesitylene and hexachloroethane, while the carbon tetrachloride solution yielded mesityl chloride and hexachloroethane. In these reactions the mercury formed calomel and corrosive sublimate, though some metallic mercury was also evolved in the chloroform solution. The equations for these reactions were as follows:

$$Mes_2H + CHCl_3 \longrightarrow 2MesH + Cl_3C-CCl_3 + Hg_2Cl_2$$

$$Mes_2Hg + CCl_4 \longrightarrow 2MesCl + Cl_3C-CCl_3 + Hg_2Cl_2.$$

The greater detachability of the mesityl radical from the Hg than was the case for the phenyl or toluene radicals was likewise observed in the reaction of dimesitylmercury with succinimide. When diphenyl- or ditoluenemercury is heated with succinimide, one radical is detached as the corresponding aromatic hydrocarbon, an aryl mercury succinimide being formed, even when the succinimide is used in excess. The same reaction

$$Mes_2Hg + HN(COCH_2)_2 \longrightarrow MesH + MesHgN(COCH_2)_2.$$

took place with dimesitylmercury, but as heating was continued, the second radical was split off as well:

$$MesHgN(COCH_2)_2 + HN(COCH_2)_2 \rightarrow MesH + Hg[N(CONH_2)_2]_2.$$

The difference between dimesityl mercury and other Ar_2Hg compounds was also manifested in catalytic decomposition reactions. When an organometallic compound of mercury is heated with finely pulverized metals, mercury is usually evolved, while the radical is dimerized. When Mes_2Hg was heated with silver, Hg was evolved; the Mes radicals did not dimerize, however, the hydrogen being rearranged, forming mesitylene and tarry products:

$$Mes_2Hg \longrightarrow Hg + MesH + (Mes\text{–}H)_n.$$

In all probability, the two methyl radicals in an ortho position to the trivalent carbon atom prevent dimerization. In this respect the catalytic decomposition of Mes_2Hg is quite similar to the decomposition of dinaphthylmercury, described by us previously [3].

EXPERIMENTAL

The Synthesis of Dimesitylmercury

116.5 g of a 3% sodium amalgam, 23.3 g of monobromomesitylene, 26 ml of anhydrous toluene, and 1.3 ml of ethyl acetate were placed in a round-bottomed flask. The mixture was heated with a reflux condenser for 14 hours over a paraffin bath to 130°, with frequent stirring. Then the hot mixture was decanted from the metallic mercury and the unreacted sodium amalgam on to a pleated filter. The dimesitylmercury residue on the filter was dissolved with boiling benzene. The finely crystalline precipitate of dimesitylmercury that settled out when the benzene cooled was filtered out. The filtrate was evaporated. The product that separated out was combined with that secured previously and recrystallized from benzene. The crystals of dimesitylmercury were washed with 95% alcohol. The dimesitylmercury was recovered as long, lustrous needles, with a m.p. of 235°, which agrees with the data given in the literature. The dimesitylmercury yield was 5.4 g, or 21.3% of the theoretical.

Photochemical Decomposition of Dimesitylmercury

These experiments were performed in sealed quartz test tubes. The light source was a PRK-2 mercury quartz lamp.

1. Dimesitylmercury and cellosolve. 2.5 g of dimesitylmercury and 20 ml of cellosolve were irradiated for 60 hours. The solution remained colorless and transparent. The deposit of metallic mercury evolved was filtered out, washed with acetone, and weighed. We secured 1.0 g of mercury, or 97% of the theoretical yield. The filtrate was fractionated with a dephlegmator into two fractions. The first fraction smelled like acetaldehyde and exhibited the qualitative reactions for aldehydes (fuchsinsulfuric acid, silver mirror). The second fraction was diluted with water, and the upper mesitylene layer was removed. We collected 0.97 g of mesitylene, or 71% of the theoretical yield. The boiling point was 165°, as determined by the Sivolobov method; the mesitylene was also nitrated to 2,4,6-trinitro-1,3,5-trimethylbenzene, with a m.p. of 233° after recrystallization from alcohol, which exhibited no depression when mixed with the pure substance.

2. Dimesitylmercury and isopropyl alcohol. 1 g of dimesitylmercury was

irradiated for 440 hours in 15 ml of isopropyl alcohol. The solution remained transparent. The deposit of metallic mercury was filtered out and washed with acetone, from which 0.05 g (5% of the theoretical) of the dimesitylmercury that had not entered into the reaction crystallized out. The metallic mercury weighed 0.42 g, or 83.3% of the theoretical. Acetone was detected in the filtrate: reaction with sodium nitroprusside and formation of the semicarbazone, m.p. 186°, exhibiting no depression when mixed with the known semicarbazone of acetone. The residue left after the acetone had been driven off was diluted with water; this yielded mesitylene, which was extracted with ether. The mesitylene recovered weighed 0.4 g (77% of the theoretical yield); it was identified as 2,4,6-trinitro-1,3,5-trimethylbenzene, with a m.p. of 233°, exhibiting no depression with the pure substance.

3. Dimesitylmercury and chloroform. 2 g of dimesitylmercury was irradiated for 130 hours in 20 ml of chloroform. The solution turned light brown. The deposit was filtered out, and it was found to contain calomel and corrosive sublimate. The deposit was washed several times with warm water to dissolve the corrosive sublimate; hydrogen sulfide was passed through the solution, and the mercuric sulfide was filtered out. The mercuric sulfide weighed 0.88 g (84% of the theoretical). The residue that was insoluble in water consisted of 0.14 g of calomel (8.2% of the theoretical) and 0.04 g of mercury (4.4% of the theoretical). Thus the mercury recovered totaled 96.6% of the theoretical yield. Mesitylene and hexchloroethane were recovered from the filtrate by distillation. The mesitylene was nitrated to 2,4,6-trinitro-1,3,5-trimethylbenzene, with a m.p. of 232°, exhibiting no depression with the pure substance. The hexachloroethane was sublimated above sulfuric acid; it had a m.p. of 186°, exhibiting no depression with the pure preparation.

4. Dimesitylmercury and carbon tetrachloride. 2.5 g of dimesitylmercury was irradiated for 150 hours in 25 ml of carbon tetrachloride. The solution turned yellow. The deposit, which consisted of calomel, was filtered out and washed with acetone. The deposit weighed 1.31 g (98% of the theoretical yield). The filtrate was distilled and found to contain hexachloroethane, m.p. 186° after sublimation above sulfuric acid, exhibiting no depression with the pure substance. The residue left after the solvent had been driven off was nitrated, the nitro product turning out to be 6-chloro-2,4-dinitro-1,3,5-trimethylbenzene, with a m.p. of 178° (recrystallized from alcohol).

No mesitylmercury chloride was found in Experiments 3 or 4.

Reaction of Dimesitylmercury with Succinimide.

Experiment 1. 2 g of dimesitylmercury and 1.1 g of succinimide were placed in a tiny flask with a sword-shaped extension, connected to a reflux condenser. The reaction lasted 3 hours, the flask being heated to 170° over a paraffin bath. The mesitylene collected in the outlet tube weighed 0.85 g (78% of the theoretical). The boiling point of the mesitylene was 162° by the Sivolobov method; the mesitylene was nitrated to 2,4,6-trinitro-1,3,5-trimethylbenzene, with a m.p. of 232° (from alcohol), which exhibited no depression with the pure preparation. The solid brown deposit on the bottom of the flask was washed repeatedly with boiling water. After it had been dissolved completely the flask was found to contain 0.02 g of metallic mercury (2% of the theoretical yield). The precipitate that settled out of the aqueous extract — minute needles — was filtered out; it was subsequently proved to be mesitylmercury succinimide. The filtrate contained ionized disuccinimide mercury, which was freely soluble in water. After a preliminary test for the mercury ion, the solution was evaporated, and the mercury was precipitated with hydrogen sulfide as mercuric sulfide. The mercuric sulfide weighed 0.62 g, corresponding to 60% of disuccinimidemercury. The mesitylmercury succinimide totaled 0.6 g, or 31.6% of the theoretical yield; it had a m.p. of 205-206° after double recrystallization from water and aqueous alcohol. Mesitylmercurysuccinimide consists of lustrous needles that are very slightly soluble in cold water, more soluble in hot water and in alcohol, freely soluble in benzene, toluene, and acetone, and very soluble in chloroform.

Table showing the Photodecomposition of Dimesitylmercury

Quantity of dimesitylmercury, g	Solvent	Irradiation time, hours	Aggregate % decomposition in terms of mercury	Decomposition products
2.5	$HOCH_2CH_2OC_2H_5$	40	97	Mesitylene, aldehyde, mercury
1	$CH_3CHOHCH_3$....	440	98.3	Mesitylene, acetone, mercury
2	$CHCl_3$	130	96.6	Mesitylene, calomel, corrosive sublimate, hexachloroethane, mercury
2.5	CCl_4	150	98	Chloromesitylene, calomel, hexachloroethane

The structure of mesitylmercury succinimide was confirmed by its reaction with hydrochloric acid. An exactly equivalent quantity of an alcoholic solution of concentrated hydrochloric acid was added to a hot water-alcohol solution of mesitylmercury succinimide. The precipitated crystals were filtered out; they fused at 200°, which agrees with the data in the literature. Adding hydrochloric acid in excess results in the formation of corrosive sublimate, which was identified by the reaction for the ion of divalent mercury.

0.1738 g substance: 0.0974 g HgS. 0.0616 g substance; 0.5896 g camphor: Δt 10°. Found %: Hg 47.90; M 418. $C_{13}H_{15}O_2NHg$. Computed %: Hg 48.04; M 417.6.

Experiment 2. This experiment was run in order to trace the course of the reaction of dimesitylmercury with succinimide with time. Heating went on for 40 minutes. Forty minutes after the start of the reaction, 0.8 g of dimesitylmercury and 0.44 g of succinimide yielded 0.23 g of mesitylene, or 52.5% of the theoretical yield. The hard white deposit in the flask was dissolved in hot water and filtered. Crystals of mesitylmercury succinimide settled out of the filtrate; they were filtered out. The yield was 0.63 g (83% of the theoretical) with a m.p. of 205-206°, exhibiting no depression with the substance investigated previously. The filtrate contained disuccinimidemercury, which was determined as mercuric chloride. The yield was 0.05 g (11.8% of the theoretical).

Catalytic Reaction of Dimesitylmercury with Metallic Silver

This reaction was performed in a small flask with a sword-shaped extension, closed by a stopper. Freshly prepared silver, made from silver nitrate and zinc, was used in these tests. 2 g of silver and 1 g of dimesitylmercury were heated to 300° over a sand bath for 3 hours. 0.34 g of mesitylene (58% of the theoretical) condensed in the outlet tube; it was identified by its boiling point of 168° (by the Sivolobov method) and by nitration. The nitroproduct was found to be 2,4,6-trinitro-1,3,5-trimethylbenzene, with a m.p. of 232° (from alcohol), exhibiting no depression with the pure substance. The tarry substances were removed from the flask with boiling benzene, though we were unable to isolate the individual substances. Reacting the metallic mercury with the silver yielded silver amalgam, the weight of mercury evolved being determined as the difference it proved to be the theoretical value. In addition, the metallic mercury sublimed from the amalgamated silver on the walls of a dry test tube (qualitative test).

SUMMARY

1. A procedure has been worked out for synthesizing dimesitylmercury from monobromomesitylene and sodium amalgam.

2. When a solution of dimesitylmercury in cellosolve is irradiated with ultraviolet light, it yields metallic mercury, mesitylene, and an aldehyde.

3. When a solution of dimesitylmercury in isopropyl alcohol is irradiated, it yields mercury, mesitylene, and acetone.

4. When a solution of dimesitylmercury in chloroform is irradiated, it is decomposed into calomel, corrosive sublimate, metallic mercury, mesitylene, and hexachloroethane.

5. When a solution of dimesitylmercury in carbon tetrachloride is irradiated, it is decomposed into calomel, chloromesitylene, and hexachloroethane.

6. When dimesitylmercury is heated with succinimide, it decomposes, the radicals being split off in two stages. The detachment of one mesityl radical as mesitylene results in the formation of mesitylmercury succinimide, which then reacts further, evolving mesitylene and disuccinimidemercury.

7. Mercury succinimide has been synthesized for the first time, a crystalline solid with a m.p. of 205-206°.

8. When dimesitylmercury is heated with metallic silver it is catalytically decomposed into metallic mercury, mesitylene, and tarry substances, produced as the result of a reaction involving the disproportionation of the radicals.

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* See CB translation p. 711 ff., 1485 ff., 1489 ff.

** See CB translation p. 183 ff., 535 ff.

REACTIONS CATALYZED BY INORGANIC HALIDES

II. THE REACTION OF ACID FLUORIDES OF CARBOXYLIC ACIDS WITH AROMATIC COMPOUNDS IN THE PRESENCE OF BORON TRIFLUORIDE

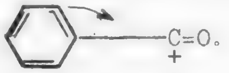
L. M. Smorgonsky

In our previous report [1] we showed that boron trifluoride is an active catalyst of the cleavage of ethers by acid halides, provided acid fluorides are used instead of acid chlorides or bromides. This was attributed to the fact that one of the essential stages of the reaction involves the coordination of the halogen atom in the acid halide to the central atom of the catalyst, and that this coordination encounters a steric hindrance when acid chlorides or bromides are employed. The catalyst's action in this reaction involves an increase in the electrophilic activity of the carbonyl carbon in the acid halide. It was only natural, therefore, for us to test the correctness of our explanation in other reactions in which the same sort of activation occurs, especially in the thoroughly investigated Friedel-Crafts reactions. We know, for example, that boron trifluoride, which is a catalyst for condensation reactions of oxygen compounds (alcohols [2], ethers [3], esters [4], and acid anhydrides [5]) with aromatic compounds, proves to be ineffective whenever we try to use alkyl or acyl chlorides in these condensations. It must be supposed that the activity of boron trifluoride as a catalyst would be manifested in these reactions as well, provided alkyl or acyl fluorides were used for condensation. This supposition is partially borne out in the paper by Burzwell and Archer [6], who have shown that cyclohexyl fluoride reacts vigorously with toluene when boron trifluoride is present, giving rise to n-cyclohexyltoluene, whereas cyclohexyl bromide and chloride do not react with toluene under these conditions.

In order to test this foregoing assumption as far as acyl halides are concerned, we undertook a study of the reaction of the acid fluorides of carboxylic acids with aromatic compounds when boron trifluoride is present. It should be noted that only very little research has been done up to now, in general, on the "ketonization" of aromatic compounds by acid fluorides. Calloway [7] has described the reaction of acetyl fluoride, and Lao-Zem-Theng and Mai [8] have described the reaction of benzoyl fluoride, with benzene in the presence of aluminum chloride. It is not impossible, however, that the actual acylating agents in these reactions are not the acid fluorides but the acid chlorides produced from the former as the result of an exchange reaction with the aluminum chloride. We may therefore state that the behavior of acid fluorides in the "pure state" in a Friedel-Crafts reaction has not been investigated thus far.

The results of the experiments described below are summarized in the following table (page 324).

In the presence of boron trifluoride most acid fluorides readily ketonize aromatic compounds, even in the cold, whereas the acid chlorides do not react with them under these conditions. The comparatively low yield of benzofuran is due to side reactions, which result in the formation of a large quantity of tarry products. In the presence of BF_3 benzoyl fluoride does not react with benzene, even when heated over a water bath, whereas benzene is ketonized by acetyl fluoride or propionyl fluoride even in the cold. Since it is highly probable that a reaction of the Friedel-Crafts type is ionic or cryptoionic, the use of a solvent with a high dielectric constant ought to promote such a reaction. Still, only traces of benzophenone was secured when benzoyl fluoride was reacted with benzene in the presence of boron trifluoride in nitrobenzene for 9 hours over a water bath. The lower reactivity of benzoyl fluoride may be due to the fact that the cationoid activity (the "electrophilia") of the carbonyl carbon atom in the benzoyl cation is reduced as the result of internal compensation.



Acid fluoride	Ketonized compound	Per cent yield of ketone	
		In terms of acid fluoride used for the reaction	In terms of the BF_3 absorbed
1. Acetyl fluoride	Benzoyl	61	80
2. Acetyl fluoride	Toluene	50	100
3. Propionyl fluoride	Benzene	36	54
4. Benzoyl fluoride	Benzene	0	0
5. Benzoyl fluoride	Toluene	67	90
6. Benzoyl fluoride	Ethylbenzene.	50	71
7. Benzoyl fluoride	m-Xylene	78	78
8. Benzoyl fluoride	Anisole	61	100
9. Benzoyl fluoride	Furan	10	29

When the boron trifluoride is replaced by its etherate, ketonization by acid fluorides requires more severe conditions, the principal reaction product being the ethyl ester of the respective acid, rather than the ketone. Thus, of the two competing reactions that the acid fluoride may enter into – the ketonization of the aromatic compound and the cleavage of the ether – the latter takes place at higher velocity. The aromatic hydrocarbon proves to be a weaker nucleophilic reagent (a "base") than the ether. It is possible that the formation of a ketone in this case is, in general, the result of a secondary reaction between the aromatic compound and the ester that is produced.

EXPERIMENTAL

The experiments described below were performed in both copper and glass vessels, the results being identical in both. The general procedure was as follows. A current of boron fluoride was passed through a mixture of the acyl fluoride and the aromatic compound, which was protected against the access of atmospheric moisture, until no more boron fluoride was absorbed. The amount of boron fluoride absorbed was determined by the gain in weight. The reaction mixture was either set aside to stand for a day at room temperature or it was kept at 40-50° for 2 hours. Then it was diluted with ether and treated with ice, and the ether layer was washed with a 10% solution of caustic soda and desiccated above magnesium sulfate. The residue left after the solvent had been driven off was fractionated.

1. Acetyl fluoride and benzene. 9 g of acetyl fluoride (0.15 mole), 25 g of benzene (0.3 mole), and 8 g of boron trifluoride (0.24 mole). Yield: 11 g of acetophenone. B.p. 77-78° at 10 mm; d_4^{20} 1.029; n_D^{20} 1.5346. Semicarbazone m.p. 200°.

2. Acetyl fluoride and toluene. 6 g of acetyl fluoride (0.1 mol), 18 g of toluene (0.2 mol), and 3.5 g of borontrifluoride (0.05 mole). Yield: 6.5 g of p-methylacetophenone. B.p. 219-220°; d_4^{20} 1.006; n_D^{20} 1.5350. Semicarbazone m.p. 196-197°.

3. Propionyl fluoride and benzene. 4.8 g of propionyl fluoride, 9.6 g of benzene, and 2.8 g of boron trifluoride. Yield: 3 g of propiophenone. B.p. 95-96° (15 mm). Semicarbazone m.p. 176°.

4. Benzoyl fluoride and toluene. 12.4 g of benzoyl fluoride (0.1 mol), 13.5 g of toluene (0.2 mol), and 5 g of boron trifluoride (0.07 mol). Yield 13.1 g of p-tolyl phenyl ketone. B.p. 180-182° (15 mm). M.p. (after recrystallization from alcohol) 54°. A test sample, mixed with the p-tolyl phenyl ketone prepared from benzoyl chloride and toluene, had the same melting point.

5. Benzoyl fluoride and ethylbenzene. 6.2 g of benzoyl fluoride (0.05 mol), 10.5 g of ethylbenzene (0.1 mol), and 4.5 g of boron trifluoride (0.07 mol). Yield: 5 g of p-ethylbenzophenone. B.p. 174-176° (10 mm), 324° (743 mm).

6. Benzoyl fluoride and m-xylene. 6.2 g of benzoyl fluoride (0.05 mol), 10 g of m-xylene (0.1 mol), and 4 g of boron trifluoride (0.06 mol). Yield: 8.2 g of 2,4-dimethylbenzophenone. B.p. 322° (743 mm); d_4^{20} 1.068; n_D^{20} 1.5915.

7. Benzoyl fluoride and anisole. 10.7 g of benzoyl fluoride, 9.3 g of anisole, and 2.7 g of boron trifluoride. A solution of the boron trifluoride in the anisole was added drop by drop to the benzoyl fluoride, with constant chilling. The reaction produced considerable heat. The mixture was set aside for a day at room temperature and then processed as in the preceding experiments. This yielded 10 g of p-methoxybenzophenone; b.p. 190-195° (10 mm); m.p. 63° after recrystallization from alcohol; a test sample mixed with the p-methoxybenzophenone prepared from benzoyl chloride and anisole, had the same melting point.

8. Benzoyl fluoride and furan. 14.5 g of benzoyl fluoride (0.12 mol) and 8 g of furan (0.12 mol) in 150 ml of absolute benzene.

A current of boron fluoride was passed through the mixture, which was chilled with an ice-salt mixture. The gain in weight was 3 g. Distillation with steam and the usual processing yielded 2 g of benzofuran; b.p. 155-157° at 12 mm.

9. Benzoyl fluoride and toluene (in the presence of boron trifluoride etherate). 6 g of benzoyl fluoride (0.05 mol), 9 g of toluene (0.1 mol), and 7 g of boron fluoride etherate were heated together for 10 hours over a water bath in a flask fitted with a reflux condenser and protected against the access of atmospheric moisture. The reaction mixture was diluted with ether and treated with ice; the ether solution was washed with a 10% solution of alkali and with water and desiccated above magnesium sulfate. The residue left after the ether and the toluene had been driven off was fractionated. This yielded 3 g of ethyl benzoate (b.p. 210-215°; n_D^{15} 1.5079) and 2 g of p-tolyl phenyl ketone (b.p. 308-310°; m.p. 52-53° after recrystallization from alcohol).

SUMMARY

The reactions of acetyl fluoride, propionyl fluoride, and benzoyl fluoride with toluene, benzene, anisole, ethylbenzene, m-xylene, and furan have been used to show that the acid halides of carboxylic acids ketonize aromatic compounds in the presence of boron fluoride, whereas the acid chlorides do not react with them under these conditions..

This is evidence that the coordination of the halogen atom in the halide constituent of the reaction with the central atom of the catalyst is an essential stage in reactions of the Friedel-Crafts type.

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DIALLYLPHOSPHOROUS ACID AND ITS DERIVATIVES

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Many dialkylphosphorous acids and their derivatives have been more or less thoroughly investigated by now. Still, the unsaturated representatives of the acid esters of phosphorous acid have not been synthesized and studied.

In 1945 V.M.Zoroastrova was the first to describe the first representative of esters of phosphorous acid containing an unsaturated radical, viz.: triallyl phosphite, in a research carried out under the supervision of A.E.Arbuzov. In 1948 the American chemist Toy [1] synthesized several diallyl aryl phosphates as follows:

$$ArPOCl_2 + 2HOCH_2{-}CH{=}CH_2 + 2C_5H_5N \rightarrow ArPO(OCH_2{-}CH{=}CH_2)_2 + 2C_5H_5N \cdot HCl.$$

The diallylphenyl phosphate he produced polymerizes with remarkable ease, forming fire-resistant copolymers with vinyl acetate, methyl methacrylate, and other unsaturated poly esters.

Recently, one of the present authors, together with N.A.Chadaeva [2], reacted phosphorous trichloride with various secondary vinyl alkyl carbinols and secured and investigated several α,α',α''-trivinyl trialkyl esters of phosphorous acid.

As far as we know, this exhausts the references in the literature to neutral as well as acid unsaturated esters of phosphorous acid. The present research was undertaken with the primary objective of synthesizing an acid ester of phosphorous acid and an unsaturated radical. We prepared diallylphosphorous acid by a method resembling that given by P. Nylan [3] for the preparation of di-ethylphosphorous acid. The reaction between absolute allyl alcohol and phosphorous trichloride proceeded smoothly and quietly as follows:

$$3CH_2{=}CH{-}CH_2OH + PCl_3 \rightarrow (CH_2{=}CH{-}CH_2O)_2POH + 2HCl + C_3H_5Cl.$$

The resultant reaction product was distilled in vacuum, but when about two-thirds of the liquid had been distilled, the remainder decomposed violently, evolving a large amount of heat and gaseous substances. This decomposition was so rapid that it nearly always ended with a very violent explosion. Upon redistillation the diallyl phosphorous acid distilled quietly and completely without decomposing. Diallylphosphorous acid is a colorless liquid with a specific odor, soluble in water, which readily adds two molecules of bromine and reacts with metallic sodium, giving rise to a sodium derivative.

We synthesized the ethyl esters of diallylphosphonoformic and diallylphosphonacetic acids:

$$(C_3H_5O)_2POCOOC_2H_5 \text{ and } (C_3H_5O_2)POCH_2COOC_2H_5.$$

by reacting the sodium derivative of diallylphosphorous acid with chlorocarbonic and chloroacetic esters.

These diallylphosphonocarboxylates are colorless liquids that are soluble in many organic solvents and, as unsaturated esters, readily add chlorine and bromine. We also attempted the preparation of diallyl phosphonoformates and diallyl phosphonoacetates in absolute ethyl alcohol. We were unable, however, to secure even a minute quantity of these phosphonocarboxylates, though we did secure diethyl carbonate with the first ester and ethoxyacetic ester with the second. In both instances, moreover, we recovered the diallylphosphorous acid. The formation of diethyl carbonate or ethoxyacetic ester may be due to the existence of the following equilibrium reaction in absolute ethyl alcohol:

$$HPO(OCH_2{-}CH{=}CH_2)_2 + CH_3CH_2ONa \rightleftarrows NaPO(OCH_2{-}CH{=}CH_2)_2 + CH_3CH_2OH.$$

When the alcohol is present in excess, the equilibrium is most likely shifted somewhat to the left, sodium ethoxide taking part in the reaction with the corresponding esters of the chloro-substituted aliphatic acids.

EXPERIMENTAL

Synthesis of diallylphosphorous acid. Diallylphosphorous acid was synthesized by a method paralleling Nylen's method. Its synthesis was effected as follows. 117 g of carefully desiccated allyl alcohol, with a b.p. of 96.5-97°, was placed in a 250 ml Arbuzov-Semenov flask. 91.9 g of freshly distilled phosphorus trichloride (based on 1 mol of phosphorus trichloride for 3 mols of allyl alcohol) was added drop by drop to the chilled alcohol, with constant stirring. The addition of each drop of phosphorus trichloride was accompanied by violent crackling and the evolution of hydrogen chloride. The reaction lasted 2 hours, carbon dioxide being passed through the mixture continuously. After all the phosphorus trichloride had been added, the chilling mixture was removed and replaced by a water bath. The flask was connected to a vacuum pump through a condenser and a receiver. The water bath was heated cautiously, causing the allyl chloride to distil and driving off the hydrogen chloride. After 3-5 hours had elapsed, the residue in the flask was distilled in a current of carbon dioxide at reduced pressure. Distillation yielded the following fractions (at 8 mm). I - up to 95°, 8 g; II - 95-98°, 52 g; and III - 98-102°, 43 g. Fractions II and III were redistilled at the same vacuum from an Arbuzov flask into a 2-bulb dephlegmator. This yielded 71 g of a fraction with a b.p. of 97.5-98.5° at 8 mm. The yield of the pure product was 65.7% of the theoretical.

Diallylphosphoruus acid is a colorless, highly mobile liquid, with a specific odor, which is freely soluble in water and in organic solvents.

d_0^8 1.1001; d_0^{20} 1.079; n_D^{20} 1.4430; MR_D 39.79; computed 39.84.
0.1253 g substance: 43.34 ml NaOH; 0.1431 g substance: 49.48 ml NaOH (1 ml NaOH = 0.5530 mg P). Found %: P 19.12, 19.11. $C_6H_{11}O_3P$. Computed %: P 19.13.

Diallylphosphorous acid readily adds two molecules of bromine. The bromine addition test was performed as follows. 1.4642 g of diallylphosphorous acid was placed in a small bottle with a ground-glass dropping funnel. Bromine was added until the slightly yellow color of the product appeared.

Bromine cnnsumed: 2.9638 g. Computed for two bonds: 2.8880 g.

Synthesis of the ethyl ester of diallylphosphonoformic acid in absolute ethyl ether. A sodium derivative of diallylphosphorous acid was placed in a 250-ml round-bottomed flask fitted with a reflux condenser, a dropping funnel and a mechanical stirrer. 3.83 g of metallic sodium in the shape of wire was placed in 100 ml of anhydrous ethyl ether, and 27 g of diallylphosphorous acid was added drop by drop, with constant stirring. The flask was chilled externally with snow during the reaction. Then the snow was removed and replaced by a water bath. After all the diallylphosphorous acid had been added, the contents of the flask were heated for 3 hours. Then the flask contents were chilled, and

18.1 g of chlorocarbonic ester was added from the dropping funnel. Then the flask was heated for about an hour over a water bath. Adding 1 ml of water caused sodium chloride to precipitate out. The next day the sodium chloride was filtered out and washed repeatedly with ether. The wash ether was combined with the filtrate. After the ether had been driven off over a water bath, the residue was distilled in vacuum. This yielded the following three fractions (at 13 mm): I – up to 151°, 6 g; II – 151-156°, 10.2 g; and III – 156-158°, 6.9 g. Fractions II and III were redistilled at 12 mm, yielding 13 g of a fraction with a b.p. of 153-154° at 12 mm, representing 33.3% of the theoretical yield.

The ethyl ester of diallylphosphonoformic acid is a colorless liquid that is soluble in ether, alcohol, benzene, and dioxane. It adds bromine readily.

d_0^0 1.1396; d_0^{20} 1.1213; n_D^{20} 1.4469; MR_D 55.53; computed 55.35.

0.1461 g substance: 34.94 ml NaOH; 0.1275 g substance: 30.47 ml NaOH (1 ml NaOH = 0.5530 mg P). Found %: P 13.22, 13.21. $C_9H_{17}O_5P$. Computed %: P 13.24.

An endeavor to prepare the anilide or the p-toluide of diallylphosphonoformic acid in crystalline form met with failure; all we got was a hyaline mass.

Action of chloroacetic ester upon the sodium derivative of diallylphosphorous acid in absolute alcohol. 2.84 g of metallic sodium was added to a 250-ml round-bottomed flask fitted with a mechanical stirrer, a dropping funnel, and a reflux condenser and containing 100 ml of absolute ethyl alcohol. 20 g of diallylphosphorous acid was added drop by drop with constant stirring to the solution of sodium ethoxide. The reaction of the sodium alcoholate with the diallylphosphorous acid was accompanied by the evolution of heat. 15.2 g of chloroacetic ester was added to the chilled solution. Then the contents of the flask were boiled for about 3 hours over a water bath. After about 50 ml of alcohol had been driven off, 100 ml of ethyl ether was added. Then the precipitate – sodium chloride, was filtered out. The solvent was driven off from the filtrate, and the residual product was distilled in vacuum. At 10 mm we collected a first fraction with a b.p. of 45-46°, d_0^0 0.9983, n_D^{20}1.4017, and a second fraction with a b.p. of 101-102°. The physical constants of the first substance were those of ethoxyacetic ester, while the second was diallylphosphorous acid. We were unable to recover the expected ester – the ethyl ester of diallylphosphonoacetic acid.

Action of chlorocarbonic ester upon the sodium derivative of diallylphosphorous acid in absolute alcohol. 80 ml of absolute ethyl alcohol was placed in the reaction flask, and 1.95 g of metallic sodium was added. 14 g of diallylphosphorous acid was added to the sodium alcoholate solution drop by drop. The reaction was accompanied by the evolution of a small amount of heat. 10 g of chlorocarbonic ester was added in small batches to the chilled solution. Toward the end, the contents of the flask were heated over a water bath for 3 hours. The further processing was like that described above; a Fraction I, representing diethyl carbonate, and a Fraction II, representing diallylphosphorous acid, were collected.

Synthesis of diallylphosphonoacetic acid in absolute ether. 120 ml of anhydrous ether and 3.83 g of metallic sodium in the shape of wire were placed in the reaction flask. 27 g of diallylphosphorous acid was added from the dropping funnel. The reaction was accompanied by the evolution of heat, so that the flask was chilled externally by snow. After 2 hours of heating, 20.5 g of chloroacetic ester (based on 1 mol of chloroacetic ester per mol of the sodium derivative of diallylphosphorous acid) was added drop by drop to the sodium derivative of the diallylphosphorous acid, the flask being chilled externally. A small amount of water was added to coagulate the colloidal sodium chloride that formed. The precipitate was filtered out on a Buchner funnel and washed three times with ether. The ether solvent was driven off, and the residual liquid was distilled at reduced pressure. The following fractions were collected (at 8 mm):

I) 144-150°, 3.8 g; II) 150-156°, 15.9 g; and III) 156-159°, 5.6 g. Redistillation of Fractions II and III yielded 12.4 g of a fraction with a b.p. of 155.5-156.5° at 8 mm. The yield was 30% of the theoretical.

The ethyl ester of diallylphosphonoacetic acid is a colorless liquid that is soluble in many organic solvents. It adds bromine readily.

d_0^0 1.1381; d_0^{20} 1.1198; n_D^{20} 1.4514; MR_D 56.68; computed 59.97.
0.1507 g substance: 34.13 ml NaOH; 0.1249 g substance: 32.19 ml NaOH
(1 ml NaOH = 0.5530 mg P). Found %: P 12.42, 12.49.
$C_{10}H_{17}O_5P$. Computed %: P 12.50.

Saponification of the ethyl ester of diallylphosphonoacetic acid. Saponification was effected by heating for 5 hours to 160° with a 20% solution of hydrochloric acid in a sealed tube. After the hydrochloric acid and the other saponification products had been removed by repeated evaporation with water, we secured a syrupy liquid, which crystallized the next day. The crystals were isolated as minute prisms after recrystallization from alcohol.

SUMMARY

1. Diallylphosphorous acid – the first representative of the unsaturated acid esters of phosphorous acid – has been synthesized and investigated for the first time.

2. Ethyldiallylphosphonoformic and diallylphosphonoacetic esters have been prepared by reacting the sodium derivative of diallylphosphorous acid with the respective esters of the chlorosubstituted aliphatic acids in a neutral solvent.

3. The formation of diethyl carbonate and of ethoxyacetic ester when the foregoing syntheses were carried out in absolute alcohol can be explained solely by assuming an equilibrium reaction between the ethyl alcohol and the sodium derivative of diallylphosphoric acid, which is shifted considerably toward the formation of sodium ethoxide.

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*See CB translation p. 1549 ff.

3-METHOXY-5-TERT-BUTYLTOLUENE

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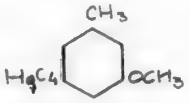
Among the derivatives of phenol or anisole, there is no description in the literature of compounds that contain a *tert*-butyl group in the meta position to the hydroxyl group. And yet, the synthesis of such compounds as 3-methoxy-5-*tert*-butyltoluene (I) would enable us to synthesize the dinitro derivative (V) and the trinitro derivative (II) by nitration; the latter two compounds ought to possess a good musk fragrance, as is evident from a comparison of the formulas of these compounds with those for the well-known xylene (III) and amber (IV) musks: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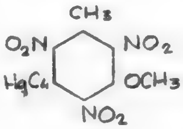
H9C4
OCH3

(I)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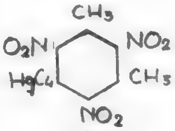
OCH3
NO2

(II)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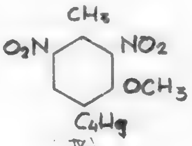
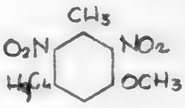
NO2
H9C4
CH3
NO2

(III)

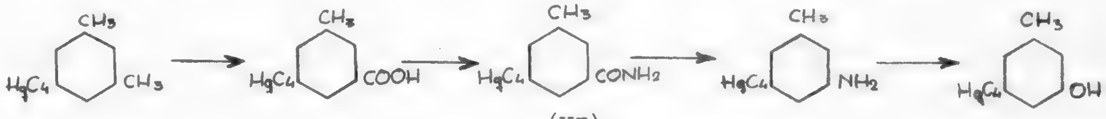

CH3
O2N
NO2
OCH3
C4H9

(IV)


CH3
O2N
NO2
H9C4
OCH3

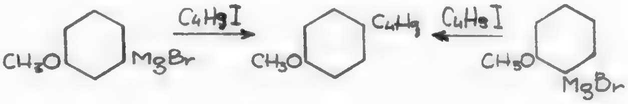
(V)

Such compounds may be synthesized in three fundamentally different ways. 1) Some group is converted into a hydroxy group, which is in the meta position to the tertiary butyl group. The readily available 3-methyl-5-tert-butyltoluene served as the raw material for an attempted synthesis by this method:


CH3
H9C4
CH3
CH3
H9C4
COOH
CH3
H9C4
CONH2
CH3
H9C4
NH2
CH3
H9C4
OH

(VI)

Experiment showed, however, that the amide (VI) cannot be converted into an amine by either the Hofmann or the Curtius reaction [1]. Chichibabin [2] encountered similar difficulties in his endeavor to convert the amide of 4-*tert*-butyl-2,6-dimethylbenzoic acid into the corresponding amine. 2) The tertiary butyl group replaces a halogen atom in the meta position to the methoxy group. Efforts to carry out this reaction by the use of organomagnesium compounds proved fruitless, owing to a singular isomerization, involving the migrating of the tert-butyl group, as has been shown by one of the present authors, [1,3].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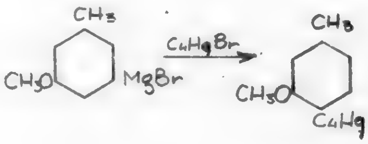
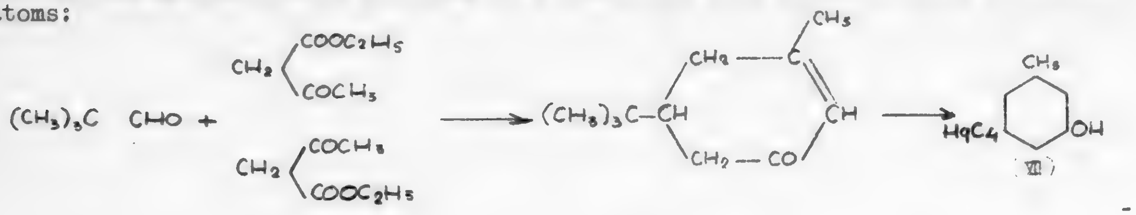
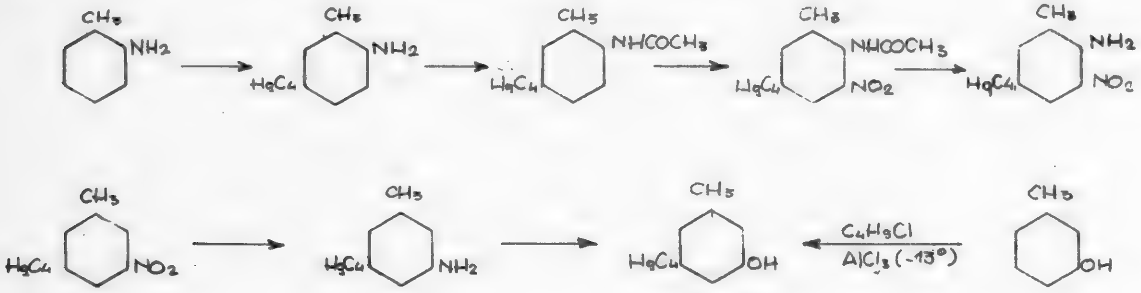
C4H9I
CH3O
MgBr
CH3O
C4H9
CH3O
MgBr


CH3
C4H9Br
CH3
CH3O
MgBr
CH3O
C4H9

3) Formation of a benzene ring with the positions of the tert-butyl and the hydroxy groups fixed, starting from compounds with an open chain of carbon atoms:

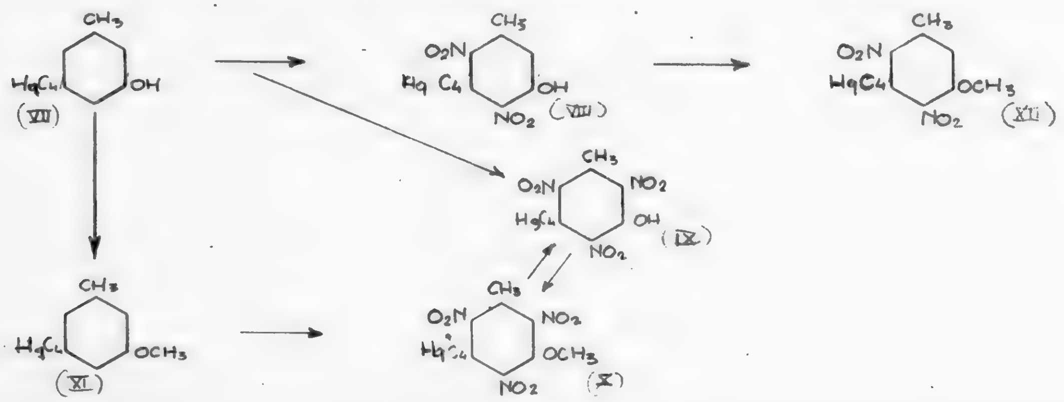


Our experiments have demonstrated, however, that trimethylacetaldehyde does not condense with acetoacetic ester, in contrast to isobutyraldehyde and p-toluylaldehyde, which condense readily with acetoacetic ester according to the foregoing simplified diagram when piperidine is present, as Knoevenagel has shown. We finally succeeded in synthesizing the desired 3-hydroxy-5-tert-butyltoluene by carrying out a long series of transformations, as shown below:



(VII)

This hydroxybutyltoluene proved to be a crystalline substance with a m.p. of 46-47°. In his last paper, published in 1942, Chichibabin [4] reported on experiments involving the condensation of tert-butyl chloride with m-cresol at low temperature (-13°) in the presence of a large quantity of aluminum chloride. He succeeded in isolating crystalline tert-butyl-m-cresol, with a m.p. of 50°, from the reaction products with good yield. He cites no data at all on the properties or structure of this substance. We repeated Chichibabin's research. The resulting crystalline tert-butyl-m-cresol had a m.p. of 48-49° and exhibited no depression when mixed in a test sample with the 3-hydroxy-5-tert-butyltoluene (VII) we had synthesized from o-toluidine. It has thus been proved that Chichibabin's tert-butyl-m-cresol is the symmetrical isomer (VII). In our subsequent experiments the substance (VII) was subjected to the following transformations:



When nitrated with dilute nitric acid, 3-hydroxy-5-butyltoluene (VII) yields a mixture of two substances (VIII)* and (IX). Substance (IX) forms a sodium salt that is slightly soluble in cold water and crystallizes readily from hot water. The Na salt of the dinitro derivative (VIII), on the other hand, is readily soluble in water. The trinitro derivative (X), a crystalline substance with a m.p. of 89°, possesses a very faint, though pleasant musk odor. This substance was synthesized in two ways: by methylating the anhydrous Na salt of Substance (IX) with dimethyl sulfate, and by nitrating Substance (XI) with nitric acid in acetic anhydride. The new musk (X) is readily demethylated by heating it with alcoholic ammonia in a sealed tube over a water bath, though it resists the action of a mixture of anhydrous nitric acid and sulfuric acid or oleum. After chromatographic purification and crystallization from alcohol, Substance (XII) consists of yellow platelets without any odor of musk.

EXPERIMENTAL.

Experiments on the condensation of trimethylacetaldehyde with acetoacetic ester. The trimethylacetaldehyde was prepared by the Danilov and Venus-Danilova method [5]. Efforts to condense the two substances without the use of a solvent, in the cold or at 45° with a few drops of piperidine present, were fruitless; the original substances were recovered in vacuum distillation. A higher temperature resulted in considerable tarring.

2-Amino-5-tert-butyltoluene. This substance was produced by the method outlined by Effront [6], with the following modifications. The mixture of isobutyl alcohol and o-toluidine hydrochloride was heated in a sealed tube to 190-200° for the first 10 hours and to 230-240° for the next 12 hours. The resulting product was purified by distilling and crystallizing its hydrochloride from dilute hydrochloric acid. The yield of the pure substance with a b.p. of 245-247° was 41.5% of the theoretical.

2-Acetamino-5-tert-butyltoluene. The method described in the literature [6] for acylating 2-amino-5-tert-butyltoluene with acetyl chloride gives a low yield of an impure product. We successfully employed a method involving acetylation by acetic anhydride in water, suggested for other amines [7]. 164 g of the base 2-amino-5-tert-butyltoluene was placed in a flask with three times its weight of water. While the flask was shaken 126 g of acetic anhydride (15% excess) was added all at once. The solution became transparent almost at once, a considerable amount of heat was evolved, and the acetyl derivative began to precipitate within a short time. The reaction mass was stirred for 15 minutes and then chilled, the precipitate being suction filtered. M.p. 161-162°. Yield 97.3% of the theoretical (200 g).

2-Acetamino-3-nitro-5-tert-butyltoluene. The method of nitrating 2-acetamino-5-tert-butyltoluene described by Baur [8] gives a negligible yield of the mononitro compound. Instead of this, we employed nitratinn in acetic anhydride. 220 g of HNO_3, sp. gr. 1.51, was added drop by drop, at 2-5° with constant stirring, to a mixture of 200 g of the synthesized acetyl derivative and 600 g of acetic anhydride. The resultant solution was poured over snow, the heavy yellow oil recovered crystallizing gradually when allowed to stand. The crystals were filtered out by suction and washed with water. M.p. 132-133° (from alcohol). Recrystallization raised the m.p. to 145°.

2-Amino-3-nitro-5-tert-butyltoluene. The method of saponifying the resulting nitro compound given in the literature [8] gives a wholly unsatisfactory yield. Satisfactory results are obtained by saponifying the substance with a mixture of formic and hydrochloric acids. A mixture of 92 g of 2-acetamino-3-nitro-5-tert-butyltoluene, 1100 ml of formic acid (b.p. 107°), and 1100 ml of concentrated hydrochloric acid was boiled for 13 hours with a reflux condenser. A red solution containing a small quantity of oily substances resulted. The solution was diluted with twice its volume of water and set aside overnight. The crystals that settled were filtered out and recrystallized from light gasoline. This yielded 52 g of brown platelets with a m.p. of 77-78°. Baur gives the m.p. of this substance as 81°.

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*It is possible that substances (VUII) and(XII) have a different arrangement of the nitro groups, viz: 2,6 or 2,4.

3-Nitro-5-tert-butyltoluene. This compound was prepared by heating a solution of the diazo compound 2-amino-3-nitro-5-tert-butyltoluene in alcohol. 154.4 g of the amino compound yielded 71.8 g of steam-distilled 3-nitro-5-tert-butyltoluene. M.p. 33°. Baur gives a m.p. of 32°.

3-Amino-5-tert-butyltoluene. This substance is not described in the literature. A mixture of 71.8 g of the nitro compound, 105 g of granulated zinc, and 24 ml of concentrated hydrochloric acid was heated over a water bath until a violent reaction set in. As the reaction died down, a total of 240 ml of acid was added in small batches. The product was distilled with steam from the alkaline solution. B.p. 133-134° (17 mm). Yield: 42.0 g. An oily liquid that darkens upon standing.

3.253 mg substance: 0.182 ml N_2 (18°, 753 mm). Found %: N 6.50.
$C_{16}H_{11}N$. Computed %: N 6.28.

3-Hydroxy-5-tert-butyltoluene. A nearly saturated solution of 19.6 g of sodium nitrite was added in the course of an hour and a half at 2-3° to the paste produced by chilling a hot solution of 42 g of 3-amino-5-tert-butyltoluene in a mixture of 550 ml of water and 65 ml of H_2SO_4, sp. gr. 1.84. The solution was filtered without allowing it to warm up. The cold filtrate was added in a fine stream to a well-stirred solution of 600 ml of H_2SO_4, sp. gr. 1.84, in 530 ml of water, heated to 140°. The resulting 3-hydroxy-5-tert-butyltoluene was distilled with steam. B.p. 232-233°, the liquid crystallizing upon standing Yield: 7.6 g. The substance was purified by heating it with 20 g of 30% NaOH solution until it dissolved and chilling it without agitation. The lower layer was decanted and the upper crystalline layer of the Na salt of hydroxybutyltoluene was pressed out, first on a glass filter, and then between sheets of filter paper. The desiccated substance was crystallized from toluene and then dissolved in 50 ml of warm water, after which the solution was acidified. The hydroxybutyltoluene distils completely at 127° and 11 mm. The substance has a m.p. of 46-47°.

3.282 mg substance; 9.700 mg CO_2; 2.875 mg H_2O. 3.162 mg substance: 9.345 mg CO_2; 2.719 mg H_2O. Found %: C 80.35, 80.52; H 9.72, 9.58.
$C_{11}H_{16}O$. Computed %; C 80.49; H 9.75.

Condensation of m-cresol with isobutyl chloride. 42 g of butyl-m-cresol, with a m.p. of 47°, was prepared from 62 g of m-cresol under the conditions described by Chichibabin [4]. A test sample, mixed with 3-hydroxy-5-tert-butyltoluene, likewise fused at 47°. Chichibabin gives the m.p. of his product as 50°.

2,4,6-Trinitro-3-hydroxy-5-tert-butyltoluene. A solution of 5 g of 3-hydroxy-5-tert-butyltoluene in 15 ml of benzene was added drop by drop to 50 ml of HNO_3, sp. gr. 1.4, chilled with ice water. After half an hour of stirring, 50 ml was added at the same temperature. The benzene layer was removed, washed with water, and agitated with 100 g of 5% KOH in a closed flask. The solid phenoxide that formed was filtered out and crystallized from 25 ml of hot water. The crystals were filtered out and dissolved in hot water, and the solution was acidified. The resultant oil (4 7 g) soon crystallized. The m.p. of the yellow lamellar needles was 104° (from alcohol).

3.106 mg substance: 0.387 ml N_2 (21°, 745 mm). 3.076 mg substance: 0.384 ml N_2 (22°, 746 mm). 0.3252 g substance: 15.10 g benzene: Δt 0.380°. Found %: N 14.05, 14 18: M 290. $C_{11}H_{13}O_7N_3$. Computed %: N 14.05; M 299.

x,x-Dinitro-3-hydroxy-5-tert-butyltoluene. The alkaline filtrate secured in the preceding experiment was acidified. The oil that formed (2.4 g) soon crystallized. Thick yellow needles with a m.p. of 103° (from aqueous methanol). A test sample exhibited considerable depression when mixed with the trinitro compound.

3.306 mg substance: 0.326 ml N_2 (21.5°, 737 mm). 3.076 mg subs., 0.305 ml N_2 (21.5°, 7.36 mm). Found %: N 11.08, 11.13. $C_{11}H_{14}O_5N_2$. Computed %: N 11.02.

0.4 g of the dinitro compound was dissolved in 15 ml of acetic anhydride, and 4 g of nitric acid, sp. gr. 1.5, was added a drop at a time at -5 to -7°. The solution grew turbid as this addition approached its end, due to the separation of minute crystals. The mixture was poured over snow, and the crystals were filtered out and twice recrystallized from alcohol. M.p. 103-104°. A test sample, mixed with 2,4,6-trinitro-3-hydroxy-5-tert-butyltoluene, exhibited no depression.

x,x-Dinitro-3-methoxy-5-tert-butyltoluene. 2.2 g of dinitrohydroxybutyltoluene was dissolved in 10 ml of methanol and then mixed with a solution of 0.2 g of sodium in 5 ml of methanol. The mixture was evaporated to dryness at 25-40°, and the resulting phenoxide was ground to a fine powder. The powder was mixed with 4 ml of anhydrous toluene and 2.7 ml of dimethyl sulfate and heated to 115-200° for 3 hours over an oil bath. The usual separation yielded a dark, tarry mass. The mass was dissolved in 50 ml of anhydrous benzene, and the solution was filtered through a column containing Al_2O_3. All the impurities were securely absorbed, the dinitromethoxytoluene passing through the column as a nearly colorless liquid. Evaporation of the benzene yielded 1.45 g of a crystalline substance. Crystallization from alcohol yielded 1.2 g of light-yellow, odorless platelets with a m.p. of 97°

3.614 mg substance: 7.135 mg CO_2; 1.992 mg H_2O. 3.340 mg substance: 0.285 ml N_2 (16.5°, 754 mm). Found %: C 53.88; H 6.17; N 9.98. $C_{12}H_{16}O_5N_2$. Computed %: C 53.72; H 5.97; N 10.22.

3-Methoxy-5-tert-butyltoluene. 10 g of 3-hydroxy-5-tert-butyltoluene was methylated with dimethyl sulfate under the usual conditions. A colorless liquid (9.8 g), with a slight odor, readily soluble in organic solvents. B.p. 225-227°.

3.424 mg substance: 10.150 mg CO_2; 3.102 mg H_2O. Found %: C 80.77; H 10.04. $C_{12}H_{18}O$. Computed %: C 80.90; H 10.11.

2,4,6-Trinitro-3-methoxy-5-tert-butyltoluene. a) 8 ml of HNO_3, sp. gr. 1.5, was added to a solution of 2 g of hydroxybutyltoluene in 15 ml of acetic anhydride that was chilled with an ice mixture. When the mixture was poured into water, a noncrystallizing oil was produced. The oil was further nitrated 5 ml of HNO_3 was added to a mixture of the oil and 25 ml of H_2SO_4, sp. gr. 1.84, chilled with ice water. Then the solution was heated to 60° and poured over ice. The precipitate was crystallized from alcohol, yielding fine, almost colorless, platelets with a m.p. of 88°. The substance has a faint odor of musk. It turns yellow fairly rapidly when exposed to light.

2.777 mg substance: 0.323 ml N_2 (21°, 750 mm). 2.802 mg subs., 0.323 ml N_2 (21°, 750 mm). 0.4260 g substance; 17.15 g benzene: Δt 0.408°. Found %: N 13.33, 13.21; M 311. $C_{12}H_{15}O_7N_3$. Computed %: N 13.42; M 313.

b) 1.4 g of 2,4,6-trinitro-3-hydroxy-5-tert-butyltoluene was methylated under the conditions specified for the preparation of x,x-dinitro-3-methoxy-5-tert-butyltoluene. The residue (1.0 g) left after the toluene had been driven off crystallized. M.p. 88°, a test sample mixed with the 2,4,6-trinitro-3-methoxy-5-tert-butyltoluene described above exhibiting no depression.

Demethylation of 2,4,6-trinitro-3-methoxy-5-tert-butyltoluene. 0.3 g of the substance was heated for 10 hours with 5 ml of a 20% solution of NH_3 in methanol in a sealed tube over a water bath until the precipitate dissolved. The alcohol was driven off, and the residue was heated with an aqueous solution of NH_3, the tar was filtered out, and the hot solution acidulated. This yielded an oil that rapidly crystallized. Nearly colorless platelets with a m.p. of 102-104° (from alcohol). A test sample, mixed with 2,4,6-trinitro-3-hydroxy-5-tert-butyltoluene exhibited no depression.

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* See CB translation p. 663 ff.

THE REACTION OF AROMATIC COMPOUNDS WITH ALLYL CHLORIDE AND ALLYL ALCOHOL IN THE PRESENCE OF ACID CATALYSTS

I. THE REACTION OF BENZENE AND TOLUENE WITH ALLYL CHLORIDE AND ALLYL BROMIDE IN THE PRESENCE OF ALUMINUM CHLORIDE

I. P. Losev, O. V. Smirnova and T. A. Pfeifer

One of the researches dealing directly with the case we are discussing, the reaction of benzene with allyl chloride in the presence of aluminum chloride, is a paper by Wispek and Zuber [1]. The authors used a Friedel-Crafts reaction to produce propylbenzene from benzene and allyl chloride. M.Konovalov and S. Dobrovolsky [2] produced 1,2-diphenylpropane from benzene and allyl chloride in the presence of aluminum chloride. The foregoing papers literally exhaust the material in the literature on the reaction of allyl chloride with benzene in the presence of aluminum chloride.

The reaction of benzene with allyl chloride in the presence of aluminum chloride is accompanied by the formation of certain reaction products, depending upon the quantitative proportions of the reacting substances. In one series of tests, for example, mono aryl derivatives were secured on the whole: benzylethylene, γ-chloropropylbenzene, and hydrindene, when the reagent proportions were 3 mols of benzene, 1 mol of allyl chloride, and 0.5 mol of $AlCl_3$ and the reaction temperature was 50°. In another instance, when the reagent proportions were 2 mols of benzene, 1/5 mol of allyl chloride, and 1/28 mol of aluminum chloride, diaryl derivatives (1,2-diphenylpropane) were secured. The formation of these products is largely related to the predominating role of the halogen or of the double bond in the allyl chloride in the reaction. When we made a study of the reaction products of the first series of tests, we found the mixture to contain γ-chloropropylbenzene, which is apparent confirmation of the greater activity of the double bond. Still, the rise of the bromine numbers to a certain limiting value (when the excess allyl chloride is removed at the start of the reaction), after which they drop, indicates that at the start of the reaction the chlorine atom reacts to form benzylethylene, which is then converted into γ-chloropropylbenzene as the result of the addition of hydrogen chloride to the benzylethylene. In fact, determination of the bromine numbers is a fairly convincing demonstratinn that the reaction follows this course. Experiments involving the determination of the bromine numbers when allyl bromide was used (instead of allyl chloride) produced no perceptible changes in the quality or quantity of the resultant products, no matter whether the reaction was carried out with benzene or with toluene. Table 1 provides the characteristics of each individual period in the reaction, thus assisting in clearing up the roles of the halogen and the double bond during the reaction. The experimental data clearly show that when the compound contains both a halogen atom and a double bond, the halogen reacts first, followed by the double bond.

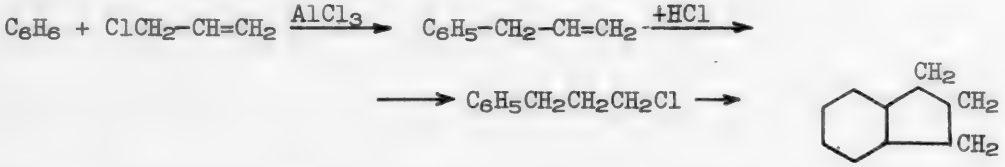
The observed decrease in the amount of hydrogen chloride evolved as the reaction progresses may likewise be considered experimental confirmation of this

TABLE 1

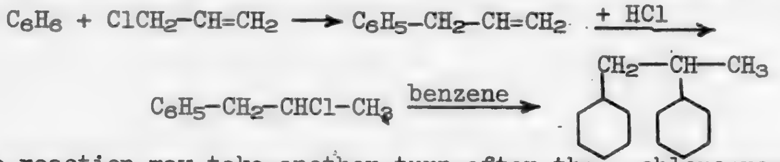
Bromine Number Determinations

Ml of allyl chloride	Bromine numbers			
	For pure allyl chloride		For the mixture of reaction products	
	Experiment 1	Experiment 2	Experiment 1	Experiment 2
1	8.8	8.7	8.8	10.0
3	12.3	11.9	12.7	14.2
5	19.0	17.9	16.6	17.7
7	20.0	21.4	19.3	18.9
9	26.1	25.9	22.1	23.5
11	29.5	27.6	35.8	33.9
13	37.5	35.8	31.7	30.8
17	48.1	46.3	22.4	23.0
21	50.8	51.0	19.1	18.8

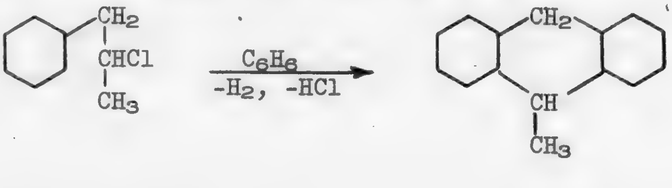
course of the reaction. The period in which there is a slight drop in the evolution of hydrogen chloride is followed by a reaction stage in which the evolution of hydrogen chloride rises again; this corresponds to the instant when the γ-chloropropylbenzene is cyclized to hydrindene. Hence, the reaction of benzene with allyl chloride (the first course taken by the reaction) may be pictured as follows:


C6H6 + ClCH2-CH=CH2
AlCl3
C6H5-CH2-CH=CH2
+HCl
C6H5CH2CH2CH2Cl
CH2
CH2
CH2

When a diaryl derivative is secured as the principal reaction product, viz.: 1,2-diphenylpropane, the equation for the reaction remains the same for the initial stage, but the addition of the HCl to the benzylethylene now is in precise conformity with Markovnikov's rule, i.e., β-chloropropylbenzene is formed. Owing to the difficulties of cyclization, the reaction follows the Friedel-Crafts' line, 1,2-diphenylpropane being formed at the expense of the halogen, the methene group of the γ-chloropropylbenzene, and another benzene molecule. The second course followed by the reaction is as follows:


C6H6 + ClCH2-CH=CH2
C6H5-CH2-CH=CH2
+ HCl
C6H5-CH2-CHCl-CH3
benzene
CH2—CH—CH3

The reaction may take another turn after the γ-chloropropylbenzene is formed, the attachment of the γ-chloropropylbenzene to the benzene molecule resulting in the formation of 9-methyl-9',10-dihydroanthracene:


CH2
CHCl
CH3
C6H6
-H2, -HCl
CH2
CH
CH3

In glancing through the literature on the reaction of toluene with halogen olefins in the presence of $AlCl_3$, we have found no comments on this subject. Assuming that the homolog of benzene—toluene will behave like the former when reacted with allyl chloride in the presence of aluminum chloride, we ran tests with toluene in which the conditions were the same as those used for benzene.

The results we obtained justify our asserting that the reaction of toluene with allyl chloride fully resembles the reaction of benzene with allyl chloride as far as the results and the mechanism of the reaction are concerned. The same holds true of the reaction of toluene with allyl bromide in the presence of aluminum chloride. The organic compounds produced had the same properties as those of the products of the reaction of allyl chloride with toluene in the presence of $AlCl_3$.

EXPERIMENTAL

First series of tests

Preparation of monoallylbenzene, o- and p-diallylbenzene, γ-chloropropylbenzene, hydrindene, 1,2-diphenylmethane, and 9-methyl-9',10-dihydroanthracene. A mixture of 234 g of anhydrous benzene (3 mols) and 66.7 g of desiccated aluminum chloride (0.5 mol) was placed in a three-necked flask fitted with a stirrer, a mercury seal, a reflux condenser, and a dropping funnel. 76.5 g of allyl chloride (1 mol) was added drop by drop to the mixture. After the mixture had been heated to 50° for 2 hours over a water bath (until no more hydrogen chloride was evolved), the reaction products were cooled, decomposed with acidified water, and set aside for 10-12 hours. Then the oily layer was separated from the aqueous layer and washed in a separatory funnel until its reaction with litmus paper was neutral. After having been washed and desiccated over calcium chloride, the reaction product was a light-yellow liquid, with blue fluorescence, that had an acrid odor. The benzene was driven off and the reaction product was distilled at atmospheric pressure, the following fractions being collected (Table 2).

TABLE 2

No. of Fraction	Boiling point	Amount of fraction recovered		Characteristics of fraction
		g	%	
I	150-200°	1.1 g	5.6	$C_6H_5CH_2CH=CH_2$, B.p. 155°; o-$C_6H_4(CH_2CH=CH_2)_2$, b.p. 94°, at 12 mm; C_9H_{10} (hydrindene), b.p. 176.5°; p-$C_6H_4(CH_2CH=CH_2)_2$, b.p. 81-83°, at 12 mm.
II	200-250	0.8	4.1	$C_6H_5CH_2CH_2CH_2Cl$, B.p. 219°.
III	250-280	1.7	8.9	
IV	280-282	2.0	10.0	1,2-Diphenylpropane, b.p. 280-282°,
V	282-300	5.2	27.2	Crystals, m.p. 79-80°; 9-monomethyl-9'10-dihydroanthracene.
VI	–	–	–	Tar

Fraction I was redistilled at atmospheric pressure. a) At a b.p. of 155-160° for the liquid, we secured a product with a b.p. of 155°, which decolorized bromine water and a permanganate solution in the cold. The liquid had an acrid odor. The molecular weight of this product was 120°, determined cryoscopically.

Found %: C 91.20, 92.11; H 8.8, 7.89. C_9H_{10}. Computed %: C 91.53; H 8.47, which are the figures for allylbenzene, $C_6H_5CH_2-CH-CH_2$.

b) We then secured a product whose boiling point was found to be 176.5°

after repeated redistillation.

d_4^{20} 0.963; n_D^{20} 1.5614. Found %: C 91.68, 92.12; H 8.32, 8.88.
C_9H_{10}. Computed %: C 91.53; H 8.47.

In view of the fact that the ultimate analysis of this product was close to that of monoallylbenzene, while its constants were close to those of hydrindene, and that it did not decolorize bromine water or potassium permanganate, its investigation was pursued still further, using bromination and ensuing oxidation of the bromide.

Bromination of hydrindene and ensuing decomposition of the bromination product. Bromination was effected with liquid bromine at 70° in chloroform. Bromination was considered terminated when no more hydrogen bromide was evolved (after 6 hours). The bromide was allowed to stand for 9-10 hours, after which it was washed in a separatory funnel with water, a weak solution of alkali, and again with water until its reaction with litmus paper was neutral. The washed bromide was desiccated above calcium chloride and then distilled at a vacuum of 50 mm. Distillation ended at 180-183°. The bromide consisted of a mixture of the two products: 1,5- and 1,6-dibromohydrindene. The bromide irritates the mucous membrane of the eye, causing burning. When it is distilled at atmospheric pressure, the bromide is decomposed, forming a product that is a less brominated derivative of hydrindene, with a b.p. of 240°. Determination of the per cent of Br indicated that this decomposition product contained 38.2% bromine, which corresponds, say, to C_9H_7Br (40.9%).

Oxidation of the decomposition product. The resultant monobromide was oxidized with a 25% solution of nitric acid above a boiling water bath. Oxidation yielded a yellow crystalline substance that is freely soluble in hot water, alcohol, chloroform, and a weak alkali solution. Double recrystallization from chloroform yielded yellowish crystals with a sublimation temperature of 105-106°.

Found %: C 43.72, 42.65; H 2.0, 1.87; Br 35.1, 35.2, (Carius):
$C_8H_3O_3Br$. Computed %: 42.32; H 1.32; Br 35.24.

which are the figures for bromophthalic acid anhydride.

Therefore, the product isolated from Fraction I, with a b.p. of 176.5°, was hydrindene.

c) When the same Fraction I was fractionated at 12 mm residual pressure, two products were recovered, one of which had a b.p. of 81-83°, and the other a b.p. of 94°. Both of these products decolorized bromine water and a permanganate solution.

Analysis of the product with a b.p. of 81-83° at 12 mm. Found %:
C 91.28, 90.87; H 8.72, 9.13; $C_{12}H_{14}$. Computed %: C 91.14; H 8.86.
Analysis of the product with a b.p. of 94° at 12 mm. Found %:
C 91.36, 91.04; H 8.64, 8.96.

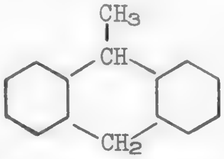
These are the figures for diallylbenzene. When we compare the boiling points of these products, we may assert that the first product is o-diallylbenzene, while the second one is p-diallylbenzene. The constants for the latter were: d_4^{20} 0.915; n_D^{20} 1.526.

Fraction II, which boiled in the 200-250° range, yielded a product with a b.p. of 219-220°, which was a saturated compound. Its Beilstein reaction for halogen was positive. When we compare the analysis data for this compound with those given in the literature, the compound in question must be called γ-chloropropylbenzene [3]. B.p. 219°; d_4^{20} 1.0801; n_D^{20} 1.5160.

Fraction III was a mixture of several substances which was hard to separate, and we were unable to recover any individual compounds from it. Fraction IV was pure 1,2-diphenylpropane, with a b.p. of 280-282°.

Found %: C 92.95, 92.14; H 7.75, 7.86: $C_{15}H_{16}$. Comp. %: C 92.84; H 8.16.

A crystalline product that distilled together with the higher fractions up to 300° was isolated from Fraction IV. The melting point of the crystals was 70 to 80°. This product was 9-methyl-9',10-dihydroanthracene.



Found %: C 92.86, 92.95; H 7.14, 7.05; $C_{15}H_{14}$. Computed %: C 92.78; H 7.22.

9-Methyl-9',10-dihydroanthracene is freely soluble in nearly all organic solvents, which renders its purification very difficult. Double recrystallization from gasoline yielded a product with a m.p. of 80-81°. Molecular weight (by the Rast method): 200; computed for $C_{15}H_{14}$: 192. Boiling the product with alcohol converted it into 9-methylanthracene [4]. The picrate of this product has the formula: $C_{15}H_{12} \cdot C_6H_3O_7N_3$. Its m.p. is 137-138° with decomposition.

Second series of tests

Preparation of 1,2-diphenylpropane. The basic reagents for this series of tests, benzene, allyl chloride, and $AlCl_3$, were used in the following proportions: 2:1/5:1/28. The mixture was stirred until a bright-red layer appeared on the surface of the liquid, indicating the formation of an intermediate compound of benzene and aluminum chloride. The intermediate compound was formed only when a current of gaseous hydrogen chloride was fed into the reaction flask at the same time the aluminum chloride was added. The contents of the flask were then allowed to cool and the allyl chloride, previously diluted with an equal quantity of benzene, was added drop by drop. The treatment of the reaction mixture was the same as that in the tests of the first series. After the benzene was driven off a product with a b.p. of 280-281° (at atmospheric pressure) and the following constants: d_4^{20} 0.981, n_D^{20} 1.558, was recovered from the reaction mixture. The product exhibited bright blue fluorescence, and was freely soluble in ethyl alcohol, acetone, and benzene. It distilled without decomposition at atmospheric pressure. The yield was 60% of the theoretical. The constants of the resultant product were those of 1,2-diphenylpropane. A series of supplementary tests were made to study its structure.

Preparation of the nitro derivatives of 1,2-diphenylpropane. The following nitrating mixture was used to nitrate 1,2-diphenylpropane: 20% HNO_3 (sp. gr. 1.51); [illegible] H_2SO_4 (sp. gr. 1.84); 13% H_2O. 3.5 g of this nitrating mixture was used for 1.9 g of the 1,2-diphenylpropane. The reaction was carried out at 50° with continuous stirring. The hydrocarbon was added to the nitrating mixture drop by drop in the course of 30 minutes, after which the mixture was stirred vigorously for 2 hours. Two products were collected after the careful fractionation of the reaction product at a residual pressure of 5 mm: a light yellow liquid with a b.p. of 133-135° at 5 mm, d_4^{20} 0.991, containing 20% NO_2, which was the mononitro derivative of 1,2 diphenylpropane.

Found %: C 73.15, 73.02; H 6.06, 6.18; N 6.7, 6.51. $C_{15}H_{15}O_2N$.
Computed % C 74.7; H 6.2; N 5.8.

The second liquid was bright orange, with a characteristic acrid odor and a b.p. of 180° at 2 mm. It contained 50% NO_2, which indicated that four nitro groups were present in the product (the theoretically calculated figure was 49%).

Found %: C 46.6, 47.8; H 3.8, 3.7; N 14.8, 14.6. $C_{15}H_{12}O_8N_4$.
Computed %: C 47.9; H 3.2; N 14.9.

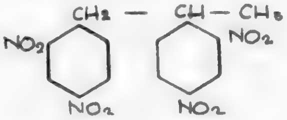
The structure of this mononitro-1,2-diphenylpropane was established by destructively oxidizing the latter: 4 g of nitrodiphenylpropane was dissolved in 80 ml of acetic acid. An oxidizing mixture, consisting of 8.6 g of $K_2Cr_2O_7$, 4.7 ml of glacial acetic acid, and 8.5 ml of water, was added* drop by drop at 60-70° to the solution of the nitro product during the course of one hour. A viscous, yellow liquid, product with a b.p. of 225-230° at 2 mm was secured after the reaction mixture had been neutralized with ammonia, the aqueous layer had been removed, and the product had been desiccated and fractionated. When the product was allowed to stand, copious quantities of acicular yellow crystals settled out, consisting of p-nitrobenzaldehyde (b.p. 106°) [5].

Found %: C 56.1, 55.2; H 3.5, 3.8; N 9.0, 9.0.
$C_7H_5O_3N$. Computed %: C 56.6; H 3.3; N 9.3.

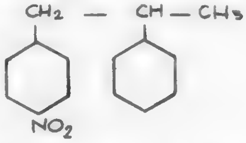
The mother liquor apparently consisted of acetophenone (a yellow liquid with a b.p. of 205-207°; d_4^{20} 1.025; n_D^{20} 1.534 [6]).

Found %: C 78.7, 79.4; H 7.2, 6.76. C_8H_8O. Computed %: C 80.0; H 6.7.

All this indicates that the structure of the nitro-1,2-diphenylpropane is:



The polynitroproduct, containing four nitro groups, has the formula:



Conversion of 1,2-diphenylpropane into 9-methyl-9',10-dihydroanthracene by distillation in the presence of $AlCl_3$. 1,2-Diphenylpropane is a rather stable compound. Repeated distillation with a view to securing a purer product, for example, indicated that when the product is present in the pure state, it distills almost completely, without decomposition. Distillation with $AlCl_3$, however, demonstrated that it could be converted into 9-methyl-9',10-dihydroanthracene. With this as our objective, 4 g of deisccated aluminum chloride was added, with constant stirring, to 5 g of 1,2-diphenylpropane. The contents of the flask were heated over a water bath for 2 hours, after which the reaction mixture was decomposed with water. Benzene was added, and the oily layer was separated from the aqueous one, desiccated with calcium chloride, and fractionated after the benzene had been driven off. A product distilled at 190-200° and 2 mm that was readily transformed into the crystalline state; repeated recrystallization from benzene yielded a crystalline substance with a m.p. of 79-80°. Determination of its constants indicated that this product was 9-methyl-9',10-dihydroanthracene.

Third series of tests

Preparation of m-allyltoluene, 7-methylhydrindene, 2',2"-dimethyl-1,2-diphenylpropane, and 2,7,9-trimethyl-9',10-dihydroanthracene. Retaining the conditions used for the reaction of toluene and allyl chloride in the presence of aluminum chloride in the first series of tests, we secured a reaction product that was separated into the following fractions by fractionation at 2 mm residual pressure (Table 3).

Repeated distillation of Fraction I yielded a product that did not decolorize bromine water, with a molecular weight of 136 and a boiling point of 182-184° at atmospheric pressure, the analysis of which corresponded to that of methylhydrindene.

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*With constant stirring.

TABLE 3

Fraction No.	Fraction boiling range at 2 mm	Amount of fraction recovered		Characteristics of fraction
		in g	in %	
I	55-100°	3.25	22.2	Equivalent to 7-methylhydrindene
II	100-135	1.25	8.4	Equivalent to m-allyltoluene
III	135-190	2.60	17.5	Equivalent to 2',2''-dimethyl-1,2-diphenylpropane
IV	190-215	5.00	33.7	Crystals: redistillation yielded 2,7,9-trimethyl-9',10-dihydroanthracene
V	215	2.70	18.2	Tar

Found %: C 91.08, 91.11; H 8.92, 8.89. Computed %: C 90.91; H 9.09.

A product with a boiling point of 197-199° at atmospheric pressure and a molecular weight of 129, the ultimate analysis of which was that of allyltoluene, was isolated from Fraction II, which decolorized bromine water and potassium permanganate.

Found %: C 89.82, 89.98; H 10.18, 10.02. $C_{10}H_{12}$. Computed %: C 90.91; H 9.09.

A product with a boiling point of 296-298° at atmospheric pressure and a molecular weight of 230 (224 was computed for $C_{17}H_{20}$) was isolated from Fraction III.

Found %: C 91.87, 91.50; H 8.13, 8.5. $C_{17}H_{20}$. Computed %: C 91.11; H 8.89.

Though the results of these analyses cannot be considered as wholly corresponding, it is nonetheless most probable that the formula of this product is 2',2''-dimethyl-1,2-diphenylpropane. Subsequent oxidation of the product, performed as was the case with 1,2-diphenylpropane, yielded toluylaldehyde.

Fraction IV was a crystalline substance, wetted with a certain amount of oil. Redistillation and repeated recrystallization from benzene yielded a crystalline product with a b.p. of 233-234° and a molecular weight of 209-212. The crystals were prisms with a yellowish tinge. Their ultimate analysis was that of trimethyldihydroanthracene.

Found %: C 92.07, 91.80; H 7.93, 8.19. $C_{17}H_{18}$. Computed %: C 91.89; H 8.11.

SUMMARY

1. The reaction of allyl chloride with benzene in the presence of desiccated aluminum chloride is a complicated one, numerous compounds being formed, the principal ones being: hydrindene, 1,2-diphenylpropane, and 9-methyl-9',10-dihydroanthracene. The intermediate products may include monoallylbenzene, p- and o-diallylbenzene, and γ-chloropropylbenzene.

2. The principal products – hydrindene and 1,2-diphenylpropane – may be secured by maintaining the appropriate quantitative proportions of the reagents. Increasing the percentage of aluminum chloride results in the synthesis of hydrindene; a cyclic compound, as the principal product, while diminishing the percentage of $AlCl_3$ entails the formation of 1,2-diphenylpropane as the principal product (up to 60% of the theoretical).

3) The reaction of benzene and allyl chloride in the presence of $AlCl_3$ takes place with the activity of the halogen in the allyl chloride (or bromide)

predominating.

4. Bromination of hydrindene with subsequent oxidation of the product of the decomposition of the dibromohydrindene results in the synthesis of bromophthalic anhydride.

5. Nitration of 1,2-diphenylpropane yielded 4'-nitro-1,2-diphenylpropane and 2', 4', 2", 4"-tetranitro-1,2-diphenylpropane.

6. Oxidation of 4'-nitro-1,2-diphenylpropane with bichromate in an acid medium yielded p-nitrobenzaldehyde and acetophenone.

7. It has been found that hydrolysis of 1,2-diphenylpropane in the presence of $AlCl_3$ results in the formation of 9-methyl-9',10-dihydroanthracene.

8. It has been found that the reaction of benzene with allyl bromide under the same conditions as those used for the reaction of benzene with allyl chloride yields the same results as the latter reaction.

9. The condensation of toluene with allyl chloride or bromide in the presence of aluminum chloride is like the reaction of benzene with allyl chloride. The principal reaction product is 2,7,9-trimethyl-9',10-dihydroanthracene. 7-Methylhydrindene and 2',2" dimethyl-1,2-diphenylpropane are by-products of this reaction.

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RESEARCH ON THE ISOMERIC TRANSFORMATIONS OF α-KETOLS

VIII. THE EFFECT OF METHYL IN THE PARA POSITION OF THE PHENYL RING UPON THE COMPARATIVE STABILITY OF ISOMERIC ALIPHATIC AROMATIC α-KETOLS

T. I. Temnikova and L. A. Petrova

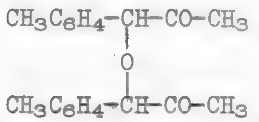
In the preceding report of this series [1] an endeavor was made to explain the influence of electronic group effects upon the comparative stability of isomeric aliphatic-aromatic α-ketols. An outline of the process involved in the reciprocal isomeric transformations of α-ketols in an alkaline medium was suggested, based upon theoretical considerations and the available experimental data.

With the objective of continuing our research on the effect of atoms and atom groups upon the equilibrium position and the velocity of the transfers in the isomeric transformations of α-ketols, we have made a study in the present report of the isomeric aliphatic-aromatic α-ketols that have a methyl group in the para position of the phenyl ring: p-tolylacetylcarbinol (I) and methyl-p-tolylcarbinol (II):

$p\text{-}CH_3C_6H_4\text{-}CHOH\text{-}CO\text{-}CH_3$; I $p\text{-}CH_3C_6H_4\text{-}CO\text{-}CHOH\text{-}CH_3$. II

We expected that the methyl group, exhibiting +I and +M effects, would cause an appreciable change in the chemical properties of the α-ketols in question as compared to their homologs that had no substitutions in the ring.

The two ketols were prepared from the corresponding α-bromoketones by heating the latter with potassium formate in methanol. When the reaction was performed with α-bromo-α-tolylacetone under the usual conditions [2], the extraordinarily high activity of the bromine atom [3] resulted in our securing a product with a high percentage of the methoxy derivative, which we were unable to separate from the ketol by fractional distillation. Only when the reaction was carried out with a saturated solution of HCOOK under unusually mild conditions were we able to secure a substance that contained no methoxy groups. The p-tolylacetylcarbinol (I) that we secured proved to be a highly unstable substance that lost one molecule of water per two molecules of the ketol more or less readily when distilled in vacuum, depending on the extent of the vacuum, and forming the crystalline product $C_{20}H_{22}O_3$. The same crystalline product is formed when the ketol is stored for a long time at room temperature, as well as by the action of acetyl chloride upon p-tolylacetylcarbinol in the presence of barium carbonate. The substance secured contains no hydroxyl groups and may be the ether of the ketol:



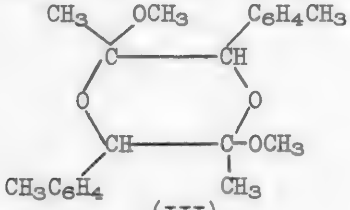
$$\begin{array}{l} CH_3C_6H_4-CH-CO-CH_3 \\ \qquad\quad\;\; | \\ \qquad\quad\;\; O \\ \qquad\quad\;\; | \\ CH_3C_6H_4-CH-CO-CH_3 \end{array}$$

Similar observations were made by A.E.Favorsky and Mandyrko [2] and A.E.

Favorsky and E.D.Venus-Danilova [2], who noticed the formation of minute quantities of such substances when the ketols they were investigating were distilled in vacuum.

A freshly distilled p-tolylacetylcarbinol produces high yields of the semicarbazone, with a m.p. of 189°, and of the osazone, with a m.p. of 141-143°. Reacting it with 2-3% HCl in methanol yields a cyclodimethyl dilactolide* with a m.p. of 253° (III).

The isomeric α-ketol – methyl-p-toluylcarbinol (II) – was prepared from α-bromoethyl-p-tolylketone by heating the latter with HCOOK and CH_3OH. The preparation secured as the result of this reaction was not the expected pure ketol, either,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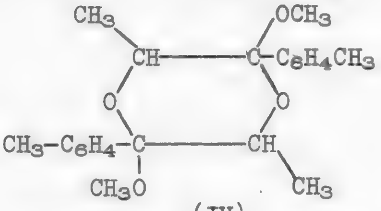
(IV)

containing the isomeric ketol p-tolylacetylcarbinol (I); the substance gave a yield of 11% of a semicarbazone corresponding to the isomeric ketol; we were unable to secure the semicarbazone corresponding to the p-toluyl isomer. The preparation was found to contain 20% of the acetyl isomer by means of titration with hydroxylamine hydrochloride. In order to prepare the pure methyl-p-toluylcarbinol, we treated the substance twice with a water-alcohol solution of semicarbazide; the resultant semicarbazone was filtered out, and the ketol was isolated from the solution in the usual manner – by slightly heating the latter with highly dilute sulfuric acid, followed by extraction with ether. The cyclodimethyl dilactolide (m.p. 230°) (IV) was prepared from the resultant substance.

Thus, we were unable to secure the pure individual isomers of the tolyl methyl ketols: the acetyl isomer (I) contained a dehydration product, apparently the ether of the ketol, while the toluyl isomer (II) was secured mixed with the acetyl isomer (I).

Since the corresponding cyclodimethyl dilactolides had been prepared from both of these ketols, we were able to solve the problem we had set ourselves in this research: ascertaining the comparative stability of these isomeric α-ketols. With this in mind, we plotted a graph showing the variation of the melting point of a mixture of the cyclodimethyl dilactolides of methyl p-tolyl ketols with the composition of the mixture (Figure, p. 747). It should be noted that as the composition of the mixture approaches the 1:1 ratio, the fusion becomes less precise, the substance beginning to soften before melting, sometimes 5-10° before the appearance of the meniscus. Lastly, the meniscus appears, and the substance clears up completely after the temperature is raised another few degrees; the temperature at which the meniscus appears is plotted on the ordinates of the graph in every instance.

The applicability of this method to the establishment of the composition of a mixture of α-ketols is shown by the formation of individual cyclodimethyl dilactolides when CH_3OH and HCl act upon the ketols, as demonstrated previously. In one of our previous reports we have also shown that the ketols are not isomerized when they are acted upon by HCl and CH_3OH in the cold, [5].

It has been shown above that the reaction of HCOOK + CH_3OH with α-bromoethyl p-tolyl ketone produces a mixture of ketols. The reaction product was treated with 3% HCl in methanol to ascertain its structure; the resultant substance fused at

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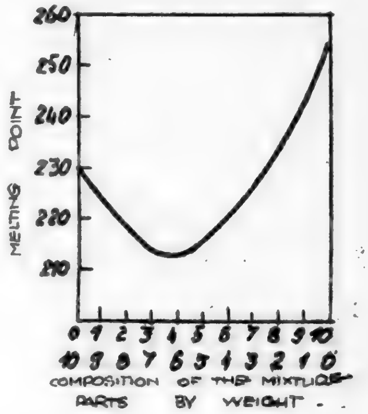
* Cf [4] for the nomenclature involved.

215-218°. When a known preparation of cyclodimethyl dilactolide is added to p-tolylacetylcarbinol, the melting point of the mixture is lowered, while it is raised when cyclodimethyl dilactolide is added to methyl-p-toluylcarbinol. With this information, we can conclude that the preparation of methyl-p-toluylcarbinol results in the formation of a mixture of ketols, which contains about 20-25% of the isomeric ketol p-tolylacetylcarbinol in addition to the normal reaction product; this agrees with the figures obtained by the hydroxylamine method. This conclusion was tested by preparing a mixture of cyclodimethyl lactolides of the specified composition – the melting point of the mixture was 218.5°.

When preparations of the ketols were heated for 20 hours with freshly precipitated barium carbonate, they isomerized, the progress of the isomerization being judged by the melting point of the resulting mixture of cyclodimethyl dilactolides. Processing of the p-tolylacetylcarbinol yielded a cyclodimethyl dilactolide with a m.p. of 227.5°; adding methyl-p-toluylcarbinol to a sample of the known cyclodimethyl dilactolide lowered the melting point, while adding a derivative of p-tolylacetylcarbinol raised it. According to the fusibility curve, these properties correspond to a lactolide mixture corresponding to 23-28% of methyl-p-toluylcarbinol and 77-72% of p-tolylacetylcarbinol; these proportions were also checked by comparison with a mixture of known proportions. In the isomerization of a ketol preparation containing 20-25% of p-tolylacetylcarbinol and 80-75% of methyl-p-toluylcarbinol, heating for 20 hours resulted in the recovery of a cyclodimethyl dilactolide with a m.p. of 226°, which is the figure for 5-10% of the acetyl isomer and 95-90% of the p-toluyl isomer.



Melting point of mixtures of cyclodimethyl dilactolide with methyl-p-toluylcarbinol and p-tolylacetylcarbinol as a function of the composition of the mixture.

These figures indicate that the toluyl isomer is the more stable of the two isomeric ketols that have a methyl and a p-toluyl group in the ketol grouping.

Composition of ketol mixture before isomerization		Composition of ketol mixture after isomerization
75-80% $p\text{-}CH_3C_6H_4COCHOHCH_3$ 25-20% $p\text{-}CH_3C_6H_4CHOHCOCH_3$	$\xrightarrow[100^\circ,\ 20\ \text{hrs.}]{BaCO_2,\ H_2O}$	90-95% $CH_3C_6H_4\text{-}CO\text{-}CHOHCH_3$ 10-5% $CH_3C_6H_4\text{-}CHOH\text{-}CO\text{-}CH_3$
100% $p\text{-}CH_3C_6H_4\text{-}CHOH\text{-}CO\text{-}CH_3$	$\xrightarrow[\text{conditions}]{\text{the same}}$	23-28% $CH_3C_6H_4COCHOHCH_3$ 77-72% $CH_3C_6H_4CHOHCOCH_3$

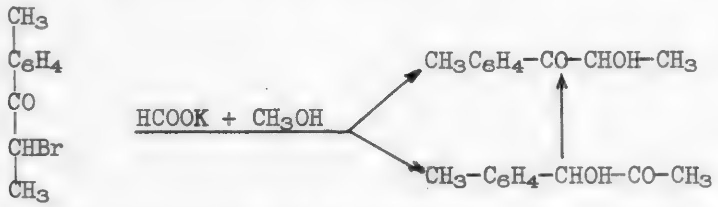
Comparison of the results of this research with the data given in the paper on the isomerization of ketols with an unsubstituted phenyl radical indicates that substituting methyl for hydrogen in the para position changes the comparative stability of the ketols, since the acetyl isomer of the homolog that has no substitution in the ring [6] is more stable:

$$C_6H_5\text{-}CO\text{-}CHOH\text{-}CH_3 \longrightarrow C_6H_5\text{-}CHOH\text{-}CO\text{-}CH_3.$$

It follows that the +M effect of the tolyl group is greater than that of the CH_3-group when these groups are present in the vicinity of an enediol grouping.

Comparison of the two papers likewise indicates how slow the isomeric transformation of methyl p-tolyl ketols is: methylbenzoylcarbinol is completely converted into the isomeric α-ketol under these conditions, while isomerization is only 20% complete in the case of the tolyl ketols. The slowness of the isomerization process when the methyl group is in the para position of the phenyl radical is further support of the outline we have suggested for the isomeric transformation of α-ketols in an alkaline medium: the increase in the electron density in the reaction zone (the zone of the CHOH-CO group) due to the +I and +M effects of the CH_3-group in the tolyl radical must slow down the prototropic process that involves the intermediate formation of an ene-diol grouping (cf the outline [1] for an alkaline medium).

In that paper it was pointed out that the reaction of HCOOK with α-bromomethyl p-tolyl ketone in methanol results in the formation of 20% of an isomeric ketol, an anomalous product of the reaction, which is less stable than the normal reaction product:



A similar phenomenon was described in the paper by T.I. Temnikova and E.I. Kulachkova for the methyl p-chlorophenyl ketols [1]; the mechanisms of this rearrangement are given in that paper.

By way of continuing previous investigations [6], we were interested in synthesizing the esters of methyl p-tolyl ketols by reacting the latter with acid chlorides. We were unable to get the reaction to proceed in the desired direction in a single case. As we have pointed out above, the reaction of tolylacetylcarbinol with acetyl chloride resulted in the formation of a dehydration product, formed from two molecules of the ketol. We were unable to secure a benzoyl derivative by reacting methyl-p-toluylcarbinol with benzoyl chloride, although the benzoic ester of a ketol is a readily identifiable substance. We prepared the latter from α-bromoethyl p-tolyl ketone and potassium benzoate as a readily crystallizable substance with a m.p. of 96-99°, which is slightly soluble in ether.

EXPERIMENTAL

1. p-Tolylacetylcarbinol

The initial p-tolylacetone and α-bromo-α-tolylacetone were prepared by the method described previously [3]. Owing to the instability of the bromoketone, it was not purified by distillation, being placed in the reaction as soon as the solvent had been driven off in vacuum. A 50% methanol solution of the bromoketone, prepared with 31 g of tolylacetone, was poured into a solution of 30 g of HCOOK in methanol that was saturated at 40°. The mixture was heated to a gentle boil with continuous stirring. The first stage of the reaction – the formation of formic ether – takes place extremely fast, though the second stage – the re-etherification stage – requires considerable time. After heating had continued for 10 hours the reaction product was processed in the usual manner.

Fractionation at 8 mm pressure yielded the following fractions: 1) b.p. 103-123°, 8.65 g; 2) 123-130°, 4.9 g; and 3) 130-133°, consisting chiefly of the ketol. The yield was 27%. The preparation of tolylacetylcarbinol thus produced was a greenish yellow liquid with a b.p. of 100-101° at 1 mm and 103-106° at 1.5-2 mm, and with an acrid odor, which quickly yields up a crystalline substance upon standing.

Analysis of the substance with a b.p. of 100-101° at 1 mm, which did not yield a crystalline substance upon standing.

> 0.0803 g substance: 0.2150 g CO_2; 0.0494 g H_2O. 0.0603 g substance: 0.1616 g CO_2; 0.0401 g H_2O. 0.1029 g substance; 17.2 g C_6H_6: Δt 0.175°; 0.1132 g substance: 20.3 g C_6H_6: Δt 0.172°. Found %: C 73.02, 73.07; H 6.88, 7.44; M 161.5, 166.3. $C_{10}H_{12}O_2$. Computed %: C 73.17; H 7.32; M 164.

Analysis of the substance distilled at low pressure (1.5-2 mm), which yielded a crystalline product upon standing, indicated a higher percentage of carbon (%C = 75.31).

Semicarbazone of tolylacetylcarbinol. This was prepared by the usual method in aqueous solution, the yield being 81% of the theoretical. It fused at 189-190° after recrystallization from alcohol.

> 0.0953 g substance: 16.0 ml N_2 (23°, 755.7 mm). 0.0921 g substance: 15.8 ml N_2 (24°, 759 mm). Found %: N 18.9, 19.0. $C_{11}H_{15}O_2N_3$. Computed %: N 19.0.

Osazone of p-tolylacetylcarbinol. A solution of 0.96 g of the ketol in a small amount of 30% acetic acid was added to a solution of 1.9 g of phenylhydrazine in 30% CH_3COOH. Prolonged agitation yielded an orange clump. After standing for 10 hours, the mixture was heated for 4 hours over a water bath (60-70°). It was poured into water 8 hours later and extracted with ether. The ether extract was desiccated with $MgSO_4$. The viscous liquid left after the ether was driven off crystallized within a month. The substance fused at 141-143° after recrystallization from alcohol.

> 0.1018 g substance: 15.0 ml N_2 (24°, 760.4 mm). 0.0767 g substance: 11.2 ml N_2 (20°, 763.4 mm). Found %: N 16.64, 16.80. $C_{22}H_{22}N_4$. Computed %: N 16.37.

Cyclodimethyl dilactolide of p-tolylacetylcarbinol. This was prepared by pouring a 2-3% solution of HCl in methane into a solution of the ketol in CH_3OH. The crystals that settled were filtered out of the solvent, washed with ether, and recrystallized from benzene. M.p. 253°.

> 0.0980 g substance: 0.2659 g CO_2; 0.0683 g H_2O. 0.1122 g substance: 0.3055 g CO_2. 0.0746 g H_2O. 0.0998 g substance: 0.1227 g AgI. 0.1023 g substance: 0.1280 g AgI. Found %: C 74.00, 74.26; H 7.80, 7.44; OCH_3 16.23, 16.54. $C_{22}H_{28}O_4$. Computed %: C 74.16; H 7.83; OCH_3 17.13.

In our initial attempts to prepare p-tolylacetylcarbinol, we used the procedure usually employed in preparing α-ketols, involving the heating of α-bromo-α-tolylacetone to 110° for 10 hours in a sealed tube with one and a half times as much HCOOK. The following principal fractions were secured: 110-112° at 12 mm. and 122-123.5° at 12 mm.

Analysis of both fractions disclosed the presence of a methoxy product (% CH_3O = 1.49 in Fraction 1 and 8.06 in Fraction 2). Each fraction yielded a semicarbazone, which proved to be a mixture of two substances: the monosemicarbazone of tolylacetone, with a m.p. of 158-161°, and the disemicarbazone of the diketone acetyltoluyl, with a m.p. of 223-224° (in a sealed tube, with decomposition), not hitherto described in the literature.

> Analysis of the substance with a m.p. of 223-224°. 0.1098 g substance: 27.9 ml N_2 (16.5°, 770.5 mm). Found %: N 30.14. $C_{12}H_{16}O_2N_6$. Computed %: N 30.43.

Investigation of the crystalline substance formed in the distillation and storage of tolylacetylcarbinol. When the freshly distilled preparation of the ketol was kept in an atmosphere of CO_2 or in sealed ampoules, it yielded a crystalline substance fairly rapidly, sometimes within $\frac{1}{2}$ - 3 hours, which consisted of elongated white prisms, with a m.p. of 173°, after recrystallization from ethyl alcohol. The lower the pressure in the system during the distillation of the ketol, the quicker the crystalline substance separated out.

0.1110 g substance: 0.3136 g CO_2; 0.0691 g H_2O. 0.0967 g substance: 0.2731 g CO_2; 0.0630 g H_2O. 0.0598 g substance; 17.7 g C_6H_6: Δt 0.065°. 0.1297 g substance; 17.1 g C_6H_6: Δt 0.145°. Found %: C 77.05, 77.02; H 6.97, 7.29; M 276, 268.5. $C_{20}H_{22}O_3$. Computed %: C 77.42; H 7.10. M 310.

The substance did not contain any OH group, nor did it form a semicarbazone.

2. Methyl-p-toluylcarbinol

The initial substance used in synthesizing methyl-p-toluylcarbinol was α-bromoethyl-p-tolyl ketone, with a m.p. of 76-77°, which is in conformity with the figures given in the literature [7]. The ketol was prepared by heating the bromoketone with HCOOK and CH_3OH to 100-110° for 10 hours in sealed tubes.

The usual processing and distillation yielded a top fraction with a boiling point that agreed with that of the expected ketol, the yield being 37% of the theoretical. B.p. 129-131° at 8 mm, 109-110° at 2 mm, and 96° at 1 mm.

0.1415 g substance: 0.3794 g CO_2; 0.0898 g H_2O. 0.1123 g substance: 0.3007 g CO_2; 0.0765 g H_2O. 0.1019 g substance: 15.4 g C_6H_6. Δt 0.203°. 0.2174 g substance: 15.4 g C_6H_6: Δt 0.445°. Found %: C 73.07, 73.11; H 7.10, 7.62; M 167, 163. $C_{10}H_{12}O_2$. Computed %: C 73.17; H 7.32; M 164.

Reacting the product with semicarbazide acetate produced a semicarbazone with a yield that was 11% of the theoretical, the m.p. of which was 188-189°, which exhibited no depression when fused with the semicarbazone of the isomeric ketol, p-tolylacetylcarbinol, which had the same melting point.

Titration with hydroxylamine hydrochloride (Marasco's method [8]). 0.3482 g substance: 5.2 ml NaOH (T 0.003513). 0.3452 g substance: 6.0 ml NaOH (T 0.003513). Found %: CH_3CO-group 21.5, 25.2.

These figures indicated that the substance prepared by reacting α-bromoethyl-p-tolyl ketone with HCOOK and CH_3OH consisted of a mixture of ketols, containing about 20-25% of the isomeric ketol p-tolylacetylcarbinol.

Cyclodimethyl dilactolide of methyl-p-toluylcarbinol. The cyclodimethyl dilactolide of the individual methyl-p-toluylcarbinol was prepared by treating a preparation of the ketol twice with a solution of semicarbazide in a water-methanol solution. The solution was set aside for two days for the semicarbazone to form and settle out completely. The filtrate was acidified with a 5% solution of H_2SO_4 and heated for a few minutes over a water bath, after which it was extracted with ether. The ether extract was washed with a soda solution and with water and desiccated with $CaCl_2$, after which the ether was driven off in vacuum. The oil that remained was covered with a 3% solution of HCl in methanol. The next day the crystalline substance that had settled was filtered out and recrystallized from a benzene-alcohol mixture. M.p. 230°.

An analysis was made for the substance secured from the ketol before the isolation of the p-tolylacetylcarbinol; (cf below.)

The Benzoyl Derivative of Methyl-p-toluylcarbinol

We were unable to secure the benzoate of the ketol by heating the ketol mixture with benzoyl chloride in benzene in the presence of $BaCO_3$.

We secured the benzoyl derivative of methyl-p-toluylcarbinol by heating

4 g of α-bromoethyl-p-tolyl ketone with 4.2 g of potassium benzoate in 60 ml of ethyl alcohol over a water bath for 8 hours. Driving off the alcohol and treating the residue with water yielded a crystalline substance that was very slightly soluble in ether; the substance had a m.p. of 96-99° after recrystallization from ligroin.

> 0.1056 g substance: 0.2956 g CO_2; 0.0604 g H_2O. 0.1113 g substance: 0.3098 g CO_2; 0.0571 g H_2O. Found %: C 76.34, 75.91; H 6.40, 5.74. $C_{18}H_{17}O_3$. Computed %: C 76.12; H 5.97.

Investigation of the Comparative Stability of α-Ketols

The isomeric transformations of the α-ketols were investigated by thermal analysis of their cyclodimethyl lactolides. The curve showing the variation of the melting point (the temperature at which a meniscus appears in the capillary) with the composition of the mixture is given in the figure.

The cyclodimethyl dilactolide of the product secured by reacting α-bromoethyl p-tolyl ketone with HCOOK in a CH_3OH solution had a m.p. of 215-218° after recrystallization from a mixture of alcohol and benzene. The first and last batches of the dilactolide had the same melting point.

> 0.0778 g substance. 0.2127 g CO_2; 0.0561 g H_2O. 0.0891 g substance: 0.2435 g CO_2; 0.0630 g H_2O. 0.1261 g substance: 0.1574 g AgI. 0.1280 g substance: 0.1598 g AgI. Found %: C 74.56, 74.53; H 8.07, 7.91; CH_3O 16.4, 16.5. $C_{22}H_{28}O_4$. Computed %: C 74.16; H 7.83; OCH_3 17.1.

Inasmuch as the melting point of the resultant dilactolide was lowered when the dilactolide of the acetyl isomer was added, and was raised when the dilactolide of the toluyl isomer was added, it follows from the curve that the ketol preparation contained 20-25% of p-tolylacetylcarbinol and 80-75% of methyl-p-toluylcarbinol.

6.4 g of this ketol mixture, with a b.p. of 110-111° at 2 mm, was heated for 20 hours over a boiling water bath with freshly prepared $BaCO_3$ while a current of CO_2 was continuously passed through the mixture. The usual isolation of the product yielded an oily liquid which was covered with a 3% solution of HCl in methanol. The resulting cyclodimethyl dilactolide fused at 226°. A mixture with the dilactolide of methyl-p-toluylcarbinol that fused at 230° had a m.p. of 227°, while its mixture with the dilactolide of p-tolylacetylcarbinol had a m.p. of 220°. From the curve we see that this means that the product secured after isomerization contained 90-95% of methyl-p-toluylcarbinol and 10-5% of p-tolylacetylcarbinol.

The preparation that consisted mainly of p-tolylacetylcarbinol (cf. p. 748) was heated to 100° for 20 hours with barium carbonate and water, with constant stirring and a current of CO_2 passed through the mixture. The substance recovered after appropriate processing was fractionated at 2 mm pressure, three fractions being collected: 88-93°, 93-98°, and 98-103°.

The action of semicarbazide acetate yielded a considerable amount of the disemicarbazide of a diketone – acetyl-p-toluyl – with a m.p. of 223-224°, from all the fractions, especially from Fraction 1.

Reacting HCl in CH_3OH (3%) with Fractions 2 and 3 yielded a cyclodimethyl dilactolide with a m.p. of 227°; a test sample mixed with the dilactolide of p-tolylacetylcarbinol fused at 245°, while a test sample mixed with the dilactolide of methyl-p-toluylcarbinol fused at 223°. The fusibility curve indicates that the lactolide mixture therefore consisted of 23-28% of methyl-p-toluylcarbinol and 72-77% of p-tolylacetylcarbinol; this was confirmed by preparing the appropriate mixture.

SUMMARY

1. The following isomeric aliphatic-aromatic α-ketols have been prepared, described as their derivatives and investigated for the first time: methyl-p-toluylcarbinol and p-tolylacetylcarbinol. It has been found that introducing a methyl group at the para position in the phenyl radical of aliphatic-aromatic α-ketols changes the properties of these ketols compared to those of homologs with unsubstituted rings, as a result of the +I and +M effects.

2. Of the two isomeric ketols, the more stable is the toluyl isomer. The isomeric transformation is much slower than in the methyl phenyl ketols. The method of thermal analysis of the cyclodimethyl dilactolides has been employed for the first time to determine the direction and extent of the isomeric transformations.

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*See CB translation p. 1323 ff.

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SYNTHESES EMPLOYING ZINC CHLORIDE

VI. THE USE OF METALLIC ZINC AND ZINC CHLORIDE FOR THE ALKYLATION OF AROMATIC COMPOUNDS OF ALKYL CHLORIDES

A. B. Kucharov

On the assumption that $ZnCl_2$ must be an extremely active catalyst at the instant of its formation, we made a study of several alkylation reactions with n-C_4H_9Cl and C_2H_5Cl in the presence of zinc dust or zinc shavings and HCl.

The use of zinc dust as a catalyst for alkylation reactions has been known for a long time; this method preceded the Friedel-Crafts synthesis. Zinke [1] and other authors [2] have described the benzylation of many aromatic hydrocarbons; some papers [3] have also described a few other instances of an alkylation reaction in the presence of zinc dust. All these syntheses have been effected by prolonged heating with considerable quantities of zinc dust (1-2 mols per mol of benzyl chloride).

In the light of the results of our previous research [4], we carried out our reaction with small quantities of zinc dust (0.015-0.03 mole per mole of the alkyl chloride). The mixture of reagents with the catalyst was saturated for so some time with anhydrous HCl (about 0.1 mole of HCl per mole of the alkyl chloride) and then heated for 5-8 hours to 230-250° in an autoclave. The reaction carried out at 120-150° yielded extremely low yields of the alkyl derivatives. Condensation tests made without any HCl produced even lower yields.

Monoalkyl derivatives are produced, with yields that attain 70-80% of the theoretical when an excess of the aromatic compound is reacted with the n-C_4H_9Cl. Reactions with C_2H_5Cl gave lower yields (50%). In these reactions the zinc dust may be replaced by zinc shavings without affecting the condensation conditions or the yields in any way. Certain new condensations using ready $ZnCl_2$ proceed in an entirely analogous fashion.

The condensation products were identified by their constants and their analyses. No precise determination was made of the structure and position of the radical in the aromatic ring, though judging by their constants, we believe that reactions with n-C_4H_9Cl yield a mixture of isomers in which the secondary butyl derivatives predominate. Condensations with n-C_4H_9Cl hardly ever occur at temperatures below 180°, though we know that tertiary C_4H_9Br alkylates naphthalene at 80-90° in the presence of $ZnCl_2$, [5]. It may therefore be supposed that in reactions involving n-C_4H_9Cl alkylation is preceded by isomerization to secondary C_4H_9Cl via the formation of an olefin and the addition of HCl to the latter. This assumption is in conformity with the data obtained in the researches of Favorsky [6] and many other authors.

EXPERIMENTAL

The reactions were carried out in a small steel acid-resistant bomb, mounted in an iron housing with a pocket for a thermometer. After the reaction was over and the bomb had cooled, the mixture was treated with water, washed, desiccated, and fractionated.

Benzene and n-butyl chloride. A mixture of 18 ml of benzene, 9.2 g of n-C_4H_9Cl, and 0.2 g of zinc dust was saturated with HCl at 5° until its gain in weight was 0.6 g; then it was heated to 230-235° for 5 hours. This yielded: 10 g (74.5% of the theoretical) of a butylbenzene fraction (160-180°); and 1.2 g (6%) of a dibutylbenzene fraction (235-245°). Repeated distillations yielded butylbenzene with a b.p. of 168-172° at 724 mm; d_{20}^{20} 0.8630; n_D^{20} 1.4896.

Found %: C 89.20; H 10.25. $C_{10}H_{14}$. Computed %: C 89.55; H 10.45.

The same reaction gave a 72% yield of butylbenzene when 0.2 g of zinc shavings was used.

Toluene and n-butyl chloride. Used: 20 ml of toluene, 9.2 g of n-C_4H_9Cl, and 0.1 g of zinc dust; 0.5 g of HCl was passed through. Heating lasted 5.5 hours at 225-230°. Fractions: 11.5 g (78%) of butyltoluene (180-200°); and 1.5 g of dibutyltoluene (240-260°).

The butyltoluene isolated had a b.p. of 190-195° at 720 mm; d_{20}^{20} 0.8650; n_D^{20} 1.4908. Found %: C 89.40; H 10.65. $C_{11}H_{16}$. Computed %: C 89.19; H 10.81.

The same reaction yielded butyltoluene (81%) without any polyalkyl derivatives when an excess of toluene was used.

Benzene and ethyl chloride. Used: 18 ml of benzene; 9.6 g of C_2H_5Cl, and 0.2 g of zinc dust; 0.4 g of HCl was passed through. Heating lasted 5 hours at 245-250°. We secured a mixture of mono- and diethylbenzenes (120-200°), totalling 10.5 g. The crude product yielded 5 g (32%) of ethylbenzene. The ethylbenzene had a b.p. of 132-136° at 722 mm; d_{20}^{20} 0.8730; n_D^{20} 1.4945.

Found %: C 90.45; H 9.25. C_8H_{10}. Computed %: C 90.56; H 9.43.

Naphthalene and n-butyl chloride. Used: 12.8 g of naphthalene, 9.2 g of n-C_4H_9Cl, and 0.2 g of zinc dust; 0.35 g of HCl was passed through. Heating lasted 6 hours at 180-190°. After the reaction was over, the excess naphthalene was driven off with steam. The oily reaction product left in the distilling flask was separated from the water, washed, desiccated with $CaCl_2$, and fractionated. This yielded 11.0 g (60%) of butylnaphthalene; and 2.5 g of dibutylnaphthalene.

The butylnaphthalene (its structure was not established) had a b.p. of 275-285° at 722 mm; d_{20}^{20} 0.9780; n_D^{20} 1.5710.

Found %: C 91.15; H 8.55. $C_{14}H_{16}$. Computed %: C 91.30; H 8.70.

Tetralin and n-butyl chloride. Used: 13.2 g of tetralin, 9.2 g of n-C_4H_9Cl, 0.1 g of zinc dust, and 0.4 g of HCl. Heating lasted 7.5 hours at 180-200°. This yielded 12.5 g (66.5%) of butyltetralin and 2.2 g of polyalkyl derivatives. The butyltetralin [7] was isolated; it had a b.p. of 265-270° at 724 mm; d_{20}^{20} 0.9385; n_D^{20} 1.5300.

Found %: C 90.00; H 10.48. $C_{14}H_{20}$. Computed %: C 89.36; H 10.64.

Carrying out the reaction with $ZnCl_2$ also gave satisfactory results. The yield of butyltetralin was 60% of the theoretical.

Bromobenzene and butyl chloride. Used: 16 g of bromobenzene (b.p. 152°), 9.2 g (0.1 mole) of n-C_4H_9Cl, and 3.4 g (0.025 mole) of $ZnCl_2$. The mixture was heated to 230-240° for 8 hours. This yielded 8.7 g (40.6%) of butylbromobenzene (a mixture of isomers) and 1.8 g of polyalkyl derivatives. Fractionation yielded a product that, judging by its physical constants [8], was secondary butylbromobenzene, with a b.p. of 228-234°; d_{20}^{20} 1.2251; n_D^{20} 1.5430.

Phenol and butyl chloride. Used: 18.8 g (0.2 mole) of phenol, 9.2 g (0.1 mole) of n-C_4H_9Cl, 0.2 g of zinc dust, and 0.2 g of HCl. Heating lasted 5 hours at 180-200°. After the reaction product had been decomposed with acidulated water, the mixture was extracted with ether, and the ether extract was treated repeatedly with 5% NaOH to extract the phenols. The alkaline solution was acidified and extracted with ether. This gave 10.6 g (70.6%) butylphenols, 2.2 g of the butyl ether of butylphenol (b.p. 245-255° at 722 mm), and 4 g of the original phenol. Fractionation of the crude butylphenol (b.p. 220-245°) yielded two fractions: secondary butylphenol [9], with a b.p. of 230-235°; d_{20}^{20} 0.9750; n_D^{20} 1.5175.

Found %: C 79.81; H 9.22. $C_{10}H_{14}O$. Computed %: C 80.00; H 9.33,

and secondary (para) butylphenol [9], with a b.p. of 240-245°; d_{20}^{20} 0.9780; n_D^{20} 1.5185.

Phenetole and butyl chloride. Used: 12 g of phenetole, 9.2 g of n-C_4H_9Cl, and 3.4 g of $ZnCl_2$. The mixture was heated for 5 hours to 180-185°. This yielded 6 g (60% of the theoretical, based on the phenetole used in the reaction) of butylphenetole, 5 g of the original phenetole, and 2 g of phenol. The secondary butylphenetole had a b.p. of 228-235°; d_{20}^{20} 0.9476; n_D^{20} 1.4958.

Found %: C 80.61; H 10.25. $C_{12}H_{18}O$. Computed %: C 80.90; H 10.11.

Condensation of toluene with n-butyl chloride in the presence of zinc. Used: 18 ml of toluene, 10 ml of n-C_4H_9Cl, and 0.2 g of zinc shavings. The mixture was heated for 4 hours in the bomb to 225-235°. This yielded 6 g (50%) of butyltoluene with a b.p. of 185-195°; d_{20}^{20} 0.8692; n_D^{20} 1.4915.

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SUMMARY

1. It has been shown that it is possible to employ small quantities of zinc and HCl for the alkylation of various aromatic compounds with alkyl chlorides.

2. The optimum reaction temperatures lie between 200 and 250°; the yield of alkyl derivatives is 50-80% of the theoretical.

3. The reactions apparently involve isomerization of the alkyl chloride radical.

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THE REACTION OF ETHYLENE SULFIDE WITH AMINES

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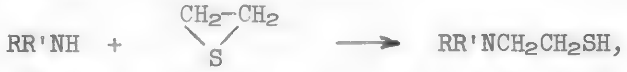
During recent years the attention of an increasing number of researchers has been attracted to the N-substituted β-aminoethanethiols. Two methods are ordinarily employed to synthesize these compounds, one involving the reaction of aminoethyl halides with hydrosulfides of the alkali metals [1], and the other being based upon the condensation of aminoethyl halides with thiourea [2]. It is only recently that Snyder and his associates [4], starting from ethylene, propylene, isobutylene, and cyclohexene sulfides and making use of the reactions between alkylene sulfides and amines described in 1936 in patent form [3], which may be represented by the following equation:



where R' = H or a radical, synthesized a number of new amino thiols and demonstrated that this is a general reaction. No matter what the nature of the amine or the alkylene sulfide used, these American authors performed the reaction under standard conditions, as follows: a mixture, usually of equimolar amounts of the alkylene sulfide and the amine, was heated to a temperature of some 100° for 16-18 hours. Using such severe conditions does not seem to be indispensable, especially when ethylene sulfide is used, and it may be undesirable or even impracticable in certain cases for one reason or another. Moreover, it is impossible to ignore the polymerization of more or less of the ethylene sulfide that always takes place under the experimental conditions, competing with the addition of the ethylene sulfide to the amine.

In this connection we describe below observations we made in our study of this reaction, using ethylene sulfide, before the publication of the paper by Snyder and his associates. These observations enable one to select the conditions to be employed in producing various β-aminoethanethiols by the foregoing method, depending upon the nature of the primary or secondary amine employed.

Delepine [5] was the first to make an attempt to secure aminothiols by the use of ethylene sulfide. Owing to the very marked tendency of ethylene sulfide to polymerize, Delepine was able to secure nothing but solid polymers containing a very low percentage of nitrogen when he reacted ethylene sulfide with aqueous or alcoholic ammonia.

As we might expect, ethylene sulfide behaves similarly with diethylamine. When freshly distilled ethylene sulfide is added at room temperature to a solution of diethylamine in methanol, a white precipitate of polymeric compounds containing no nitrogen begins to settle out within a few minutes, the precipitation being complete within a few hours. The polymerization of even small quantities of ethylene sulfide under these conditions is so obvious and so complete that this reaction may be recommended for its quantitative determination.

We know that ethylene sulfide is unstable, gradually being transformed into polymers even when stored under standard conditions. But the polymerization of ethylene sulfide is incomparably faster in the presence of diethylamine in methanol, comparable to what takes place when a solution of alkali is added. It would seem to be obvious that such rapid polymerization of ethylene sulfide, as a result of which it escapes from a reaction with diethylamine, is due to the presence of an ionizing solvent. And, indeed, when ethylene sulfide is reacted with an excess of diethylamine at room temperature for 4 days, with no methanol present, polymers are formed, true enough, but they total only 20% by weight of the ethylene sulfide used. What is more, we are able to recover the previously described β-diethylaminoethanethiol from the reaction solution, its yield being 41% of the theoretical, based on the ethylene sulfide. When the reaction is carried out in absolute ether or benzene, the polymerization of the ethylene sulfide is suppressed practically completely, and the yield of the aminothiol increases appreciably. When 0.1 mol of ethylene sulfide is added to 0.2 mol of diethylamine in 20 ml of absolute ether, for instance, and the solution is allowed to stand for 4 days, the yield of β-diethylaminoethanethiol is 55-57% after fractionation in vacuum in a current of nitrogen. Lastly, accelerating the reaction by heating the solution to 100° makes it possible to attain an even more complete addition of the ethylene sulfide to the diethylamine within as little as 2 hours. The yield of the diethylaminoethanethiol is 75-80%, this yield rising no higher when heating is prolonged beyond that time.

Ethylene sulfide reacts smoothly with other amines that are strong and medium-strength bases under analogous conditions, i.e., heating to about 100° for 2 hours in a solution of absolute benzene. These amines include: di-isoamylamine, n-hexylamine, diallylamine, N,N-diethylethylenediamine, benzylamine, and morpholine, the products comprising the corresponding β-aminoethanethiols substituted at the nitrogen atom.

When ethylene sulfide is heated in a benzene solution with as weak a base as aniline, the reaction is quite incomplete when carried out under the conditions specified above, much of the ethylene sulfide remaining unchanged, as may be readily proved by means of the following test: 1 ml of the benzene fraction of the reaction solution, driven off over a water bath in a current of nitrogen, is mixed with an equal volume of diethylamine and 2-3 ml of methanol and then boiled for a few minutes; a bulky precipitate of the polymerization products of ethylene sulfide soon begins to settle out. We later learned that only a small part of the ethylene sulfide polymerizes when mixed with an excess of aniline, even when no inert solvent is present. Fractionation of such a solution in a current of nitrogen after it had stood for 5 days at room temperature produced a yield of 60% of β-phenylaminoethanethiol. The same result may be achieved by heating 1 mol of ethylene sulfide with 2 mols of aniline to 100° for as little as 2 hours. Fractionation of the reaction solution yields, in addition to the phenylaminoethanethiol, a small quantity of a substance that is the product of the reaction of 2 mols of ethylene sulfide with aniline, to judge by its percentage of sulfur. The results of potentiometric determination of the sulfhydryl group in this compound justifies our assuming that it is β-phenylaminoethyl-β-mercaptoethyl sulfide, $C_6H_5NHCH_2CH_2SCH_2CH_2SH$. Snyder and his associates [4] ascribe the structure of a di-(β-mercaptoethyl)-aniline to this compound, though they advance no proof of this assertion.

The reaction between ethylene sulfide and aniline, in contrast to the reaction with diethylamine, may be performed even in an ionizing solvent with satisfactory results.

The aminothiols described in the present paper are colorless, transparent liquids with a disgusting odor, which mix with the usual organic solvents and undergo rapid changes when exposed to atmospheric oxygen. Some of the synthesized aminothiols were converted into hydrochlorides for further identification.

E.N.Markacheva assisted in this research.

EXPERIMENTAL

Ethylene sulfide [6]. A solution of 90 g of potassium thiocyanate in an equal quantity of water was placed in a 350 ml three-necked flask fitted with a thermometer, a mechanical stirrer, and a gas-supply tube, and an even stream of ethylene oxide was passed through the mixture for 4 hours at -5 to -7°, with constant stirring until the contents of the flask had gained 70 g in weight. The contents were then stirred at the same temperature for another 3 hours. The transparent reaction solution, which had begun to layer toward the end of this period, was set aside to stand at 0 to +3° until the following morning, 3-4 drops of benzenethiol having first been added to stabilize the ethylene sulfide [7]. Then the liquid was decanted from the precipitate produced with potassium cyanide, filtering the liquid if necessary to remove suspended particles, and the considerably increased top layer was separated and washed three times with a 20% solution of sodium chloride, using 45 ml of the salt solution for each washing. A few drops of benzenethiol were again added to the crude ethylene sulfide thus processed, and it was desiccated above calcium chloride and fractionated into a 25-cm herringbone dephlegmator, the 53.5-55° fraction being collected. The yield of ethylene sulfide totaled 23.3 g, or about 50% of the theoretical. The ethylene sulfide prepared in this manner remained transparent for 3-4 days. To keep the ethylene sulfide for a longer time, say a month or so, the freshly prepared substance must be stabilized by adding 1 drop of benzenethiol to every 6 g or by dissolving it in 2.5 times its volume of benzene. The benzene solution may then be used for research. The potassium cyanate produced in the reaction, contaminated with polymeric sulfur compounds, weighed about 20 g after being washed with alcohol and desiccated.

β-Diethylaminoethanethiol. A) 6 g (0.1 mol) of ethylene sulfide was added to a mixture of 20.5 ml (0.2 mol) of diethylamine and 20 ml of absolute ether, chilled with ice water, and allowed to stand at room temperature for 4 days. During this time a small quantity of colorless polymers gradually settled out of the initially transparent reaction solution. The solution was transferred to a Claisen flask connected to a short herringbone dephlegmator and fractionated in a current of nitrogen, fractionation being done in vacuum toward the end. The 61-65° fraction at 23 mm was diethylaminoethanethiol. The yield was 7.6 g, or 57% of the theoretical, based on the ethylene sulfide. When redistilled nearly all the diethylaminoethanethiol distilled over at 55° (17 mm); n_D^{20} 1.4665.

0.2769 g substance: 0.4845 g $BaSO_4$. Found %: S 24.0. $C_6H_{15}NS$. Computed %: S 24.07.

B) A water-chilled solution of 6 g of ethylene sulfide in 15 ml of absolute benzene was mixed with 20 ml of diethylamine in 10 ml of benzene, placed in a tube that was sealed, and heated to about 100° in a furnace for 2 hours. The next day the reaction solution was decanted from the thin polymer film that adhered to the walls of the tube and fractionated in a current of nitrogen.

The yield of diethylaminoethanethiol, collected at 64-65° (24 mm), was 10.7 g, or 80%.

β-Di-isoamylaminoethanethiol. 6 g of ethylene sulfide was chilled and poured into a chilled solution of 31.4 g of di-isoamylamine (b.p. 184-190°) in 25 ml of absolute benzene, placed in an autoclave made of ĒYa1-T steel, with a capacity of 100 ml, and heated for 2 hours over an oil bath whose temperature was about 100°. The next day the reaction mixture was fractionated in vacuum in a current of nitrogen. The yield of di-isoamylaminoethanethiol, collected at

100-110° and 4 mm, totaled 14.1 g, or 65%. The di-isoamylaminoethanethiol was redistilled for analysis.

B.p. 104-105° at 5 mm; d_4^{20} 0.8659; n_D^{20} 1.4611; MR_D 68.82; computed 69.25.

0.1983 g substance: 0.2129 g $BaSO_4$. Found %: S 14.74.
$C_{12}H_{27}NS$. Computed %: S 14.76.

1 g of pure di-isoamylaminoethanethiol was dissolved in 15 ml of anhydrous ether, and 0.8 ml of a 25% solution of HCl in absolute alcohol was added to the solution, which was chilled with ice water. The hydrochloride precipitate was filtered out 1 hour later, dried in vacuum, and recrystallized from ethyl acetate. Colorless prisms with a m.p. of 107-109°.

0.1182 g substance: 0.0667 g AgCl. Found %: Cl 13.96.
$C_{12}H_{28}NClS$. Computed %: Cl 13.97.

β-n-Hexylaminoethanethiol. 6 g of ethylene sulfide in 15 ml of absolute benzene was chilled and added to a chilled solution of 20.2 g of n-hexylamine in 10 ml of absolute benzene; the mixture was placed in a 100-ml steel autoclave and heated for 2 hours over an oil bath whose temperature was about 100°. The yield of hexylaminoethanethiol, collected at 95-100° and 6 mm, totaled 9.4 g, or 58%. The pure substance had a b.p. of 102-103° at 9 mm.

d_4^{20} 0.8937; n_D^{20} 1.4700; MR_D 50.33; computed 50.43.

0.2232 g substance: 0.3264 g $BaSO_4$; Found %: S 20.08.
$C_8H_{19}NS$. Computed %: S 19.89.

1.6 g of hexylaminoethanethiol was dissolved in 20 ml of anhydrous ether, chilled, and an 18.5% solution of HCl in absolute alcohol was added until the whole reacted acid to Congo red. The resultant precipitate was recrystallized from absolute alcohol. Silvery lamellae with a decomp. temp. of 260-261° (6° per minute).

0.0605 g substance: 3.09 ml 0.1 N $AgNO_3$. Found %: Cl 18.11.
$C_8H_{20}NClS$. Computed %: Cl 17.94.

β-Diallylaminoethanethiol. 6 g of ethylene sulfide was heated with 19.4 g of diallylamine (b.p. 108-112°) and 25 ml of absolute benzene under the conditions specified for the synthesis of the di-isoamylaminoethanethiol. The yield of the diallylaminoethanethiol, collected at 83-87° and 14 mm, ranged from 68 to 74%. The pure substance had a b.p. of 83-84° at 14 mm.

d_4^{20} 0.9411; n_D^{20} 1.4970; MR_D 48.87; computed 49.84.

0.1695 g substance: 0.2502 g $BaSO_4$. Found %: S 20.27.
$C_8H_{15}NS$. Computed %: S 20.40.

N,N-Diethyl-N'-β-mercaptoethylethylenediamine. 23.2 g of N,N-diethylethylenediamine was chilled and mixed with 6 g of ethylene sulfide in 25 ml of chilled absolute benzene. The resulting solution, which soon began to grow cloudy even at room temperature, was heated to 100-105° for 2 hours in two sealed ampoules. In contrast to the results secured when the reaction was carried out under the same conditions but using other amines, the reaction solution contained a considerable quantity of polymer compounds. Fractionation in a current of nitrogen in vacuum yielded 8.2 g, or 40% of N,N-diethyl-N'-β-mercaptoethylethylenediamine, which distilled at 92-97° and 5 mm. The aminothiol was redistilled for analysis.

B.p. 92-93° at 5 mm; d_4^{20} 0.9264; n_D^{20} 1.4795; MR_D 53.99; computed 54.38.

0.1823 g substance: 0.2370 g $BaSO_4$. 0.0206 g substance; 11.5 ml 0.01 N $AgNO_3$ (potentiometrically) [8]. Found %: S 17.85; S in the SH group 17.90.
$C_8H_{20}N_2S$. Computed %: S 18.19.

It should be noted that in one of the tests, when the N,N-diethylethylene diamine was mixed with the ethylene sulfide in a tube at 0° with no inert solvent present, sudden polymerization set in after the tube was sealed and the solution had reached room temperature, accompanied by the evolution of considerable heat. We were unable to recover the expected N,N-diethyl-N'-β-mercaptoethylethylenediamine from the reaction mixture after heating for 2 hours at 100°.

When N,N-diethyl-N'-β-mercaptoethylethylenediamine was dissolved in anhydrous ether and a solution of hydrogen chloride in absolute ethyl alcohol was added, we secured a semisolid substance that did not crystallize.

β-Benzylaminoethanethiol. This was synthesized under the same conditions as those described above for di-isoamylaminoethanethiol. The yield was 68%.

B.p. 121-123° at 6 mm; d_4^{20} 1.0563; n_D^{20} 1.5614; MR_D 51.28. Computed 51.46.

0.1930 g substance: 0.2687 g $BaSO_4$. Found %: S 19.11. $C_9H_{13}NS$. Computed %: S 19.18.

The hydrochloride of the benzylaminoethanethiol, prepared by adding an alcoholic solution of HCl to an ether solution of the aminothiol, was recrystallized from aqueous alcohol, after which it consisted of colorless prisms that fused at 260-261° (6° per minute) with decomposition and preliminary darkening.

0.1342 g substance: 0.0934 g AgCl. Found %: Cl 17.22.
$C_9H_{14}NClS$. Computed %: Cl 17.41.

β-Phenylaminoethanethiol. 6 g of ethylene sulfide was mixed with 18.6 g of aniline, and the resulting solution was allowed to stand for 5 days at room temperature. Toward the end of this time an extremely small quantity of polymer compounds settled out of the transparent solution. Fractionation in vacuum in a current of nitrogen yielded 9.3 g, or 60%, of phenylaminoethanethiol, collected at 141-151° and 14-15 mm. The phenylaminoethanethiol may be prepared with the same yield by heating 1 mol of ethylene sulfide with 2 mols of aniline to 100° in an autoclave for 2 hours.

B.p. 138-139° at 12 mm; d_4^{20} 1.1011; n_D^{20} 1.6057.

0.2102 g substance: 0.3147 g $BaSO_4$. 9.049 mg substance: 6.0 ml 0.01 N H_2SO_4 (Kjeldahl). Found %: S 20.65; N 9.28.
$C_8H_{11}NS$. Computed %: S 20.93; N 9.15.

Fractionation of the reaction solution yielded a small quantity of a fraction with a much higher boiling point, in addition to the phenylaminoethanethiol. We were able to isolate a thick, oily substance, with a b.p. of 182-185° at 4 mm, by repeated distillation in nitrogen of this fraction, accumulated in a number of tests. The analysis data indicate that this substance is β-phenylaminoethyl-β'-mercaptoethyl sulfide, $C_6H_5NHCH_2CH_2SCH_2CH_2SH$.

0.1895 g substance: 0.4103 g $BaSO_4$. 0.0385 g substance: 18.26 ml 0.01 N $AgNO_3$ (potentiometrically). Found %: S 29.73; S in SH group 15.21.
$C_{10}H_{15}NS_2$. Computed %: S 30.07; S in SH group 15.03.

Condensation of the phenylaminoethanethiol with 2,4-dinitrochlorobenzene in absolute alcohol with sodium hydroxide [9] yielded β-phenylaminoethyl-2,4-dinitrophenyl sulfide, which had a m.p. of 168.5-169.5° after recrystallization from isoamyl alcohol (1:175).

3.443 mg substance: 6.721 mg CO_2; 1.271 mg H_2O. Found %: C 53.23; H 4.13.
$C_{14}H_{13}O_4N_3S$. Computed %: C 52.64; H 4.10.

β-Morpholine-ethanethiol. 6 g of ethylene sulfide, chilled, was added to a chilled solution of 17.4 g of morpholine in 25 ml of anhydrous benzene, the resultant solution was placed in a 100-ml steel autoclave and heated for 2 hours over an oil bath whose temperature was about 100°. Fractionation in a current of nitrogen yielded 12.2 g, or 83%, of morpholine-ethanethiol, collected at 73-80° and 4 mm. The aminothiol was redistilled for analysis.

B.p. 77-79° at 5 mm; d_4^{20} 1.0670; n_D^{20} 1.5033; MR_D 40.80. Computed 40.98.

0.2010 g substance: 0.3132 g $BaSO_4$. 0.0272 g substance: 17.75 ml 0.01 N $AgNO_3$, (potentiometrically). Found %: S 21.39; S in the SH groups 20.92. $C_6H_{13}ONS$. Computed %: S 21.78.

1.5 g of morpholine-ethanethiol was dissolved in 20 ml of anhydrous ether, chilled with ice water, and an approximately 20% solution of HCl in absolute alcohol was added until the reaction of the mixture was acid with Congo red. The precipitate that settled was washed with anhydrous ether and desiccated. It weighed 2 g; m.p. 148-152°. The hydrochloride had a m.p. of 150-152° after a single recrystallization from an alcohol-ether mixture. Repeating the recrystallization, however, caused the melting point to rise sharply to 211-223°. This seems to indicate that recrystallization of the aminothiol hydrochloride involved its oxidation to a disulfide.

0.1393 g, 0.1359 g substance: 0.1095 g, 0.1060 g AgCl. Found %: Cl 19.44, 19.30. $C_6H_{14}ONClS$. Computed %: Cl 19.31 $C_{12}H_{26}O_2N_2Cl_2S_2$. Computed %: Cl 19.42.

SUMMARY

1. When ethylene sulfide is reacted with primary and secondary amines, formation of an aminothiol competes with polymerization of the ethylene sulfide.

2. Ethylene sulfide is polymerized completely in the presence of a solution of an amine that is a strong base in an ionizing solvent, thus evading a reaction with the amine.

3. It is advisable to carry out the reaction in an indifferent solvent in order to suppress the polymerization of ethylene sulfide in the reaction with primary or secondary amines that are strong or medium-strength bases.

4. Only a minute percentage of the ethylene sulfide is polymerized in the presence of a base as weak as aniline. The addition of ethylene sulfide to aniline takes place smoothly at room temperature or when heated, provided no indifferent solvent is present.

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THE MECHANISM OF THE OXIDATION OF ORGANIC COMPOUNDS BY SELENIUM DIOXIDE

XII. THE OXIDATION OF NAPHTHYLACETONITRILE AND THE ESTERS OF NAPHTHYLACETIC ACID

N. N. Melnikov and Yu. A. Baskakov

As we know, employing selenium dioxide to oxidize various classes of organic compounds has yielded many interesting results of general and preparative importance.

By now studies have been made of the oxidation of a large number of organic compounds with this oxidant [1-7]. A specific feature of selenium dioxide as an oxidizing agent is its action upon a methyl or methylene group attached to a radical activated by the ionization of hydrogen. The carbonyl group exerts the greatest effect, that of an aromatic hydrocarbon radical or of radicals of heterocyclic nitrogen compounds being much weaker, so that the latter two classes of compounds are oxidized at higher temperatures [1-9]. In the light of this, we were interested in making a study of the selenium-dioxide oxidation of the nitriles of acids that ought to occupy an intermediate position between carbonyl compounds and heterocyclic nitrogen compounds according to the activity of the hydrogen atoms in their α-methylene group. We used α-naphthylacetonitrile in our study of this reaction, as it is a readily available compound and is easily prepared from naphthylchloromethane. We also ran tests on oxidizing the methyl and ethyl esters of naphthylacetic acid and naphthylchloromethane with selenium dioxide. These tests indicated that naphthylacetonitrile is oxidized violently at about 180°, the principal reaction product being a nitrile of naphthoylformic acid, i.e., the reaction is as follows:

$$C_{10}H_7CH_2CN + SeO_2 \quad = \quad C_{10}H_7COCN + Se + H_2O.$$

In addition to the nitrile of naphthoylformic acid, a certain amount of naphthoic acid is formed; this is, apparently, a by-product resulting from the hydrolysis of the nitrile of naphthoylformic acid by water:

$$C_{10}H_7COCN + H_2O \quad = \quad C_{10}H_7COOH + HCN.$$

Despite the existence of this side reaction, the yield of the nitrile of naphthoylformic acid is more than 60%, based on the naphthylacetonitrile placed in the reaction, so that this may be employed as a preparative reaction. The esters of naphthylacetic acid are oxidized similarly, the principal reaction products being esters of naphthoylformic acid (the yield exceeding 70%), with a trace of naphthoic acid:

$$C_{10}H_7CH_2COOR + SeO_2 \quad = \quad C_{10}H_7COCOOR + H_2O + Se.$$

We were unable to isolate the individual products of the reaction between naphthylchloromethane and selenium dioxide, inasmuch as tarring, with molecular condensation, set in, even at low temperature.

EXPERIMENTAL

1. Oxidation of α-naphthylacetonitrile. 11.1 g of freshly sublimed selenium dioxide, ground to a fine powder, was added to 16.7 g of α-naphthylacetonitrile, and the mixture was heated, with stirring, in a flask with a reflux condenser, over a metal bath. When the bath temperature reached 180°, a violent reaction set in, with foaming. After the violent reaction had subsided, the reaction mixture was heated to 180-200° for another 20 minutes. Hydrocyanic acid was evolved during the reaction, as was proved by appropriate reactions. The reaction mass was cooled, 50 ml of ether was added, and the selenium was filtered out. The selenium was washed with water and desiccated, the yield being 6 g (78%). The ether solution was twice extracted with a saturated solution of soda, the ether was driven off, and the residue was treated with bisulfite. No bisulfite compound of an aldehyde was found, however. The residue was redissolved in ether, the ether solution was washed with water and desiccated above magnesium sulfate, and the ether was driven off. The residue was fractionated in vacuum. Vacuum fractionation yielded 4 g of the unreacted α-naphthylacetonitrile (24%), with a b.p. of 195-198° at 20 mm, and 8.5 g of the nitrile of naphthoylformic acid (47%), with a b.p. of 165-170° at 20 mm. The m.p. of the nitrile of α-naphthoylformic acid was 100-101° after double recrystallization from petroleum ether. This nitrile has a m.p. of 101° according to the literature [8].

0.3422 g and 0.3208 g substance; consumed to bind the ammonia: 17.89 and 17.09 ml 0.1 $\underline{N}$ H_2SO_4. Found %: N 7.32, 7.45. $C_{12}H_7ON$. Computed %: N 7.7.

Acidification of the soda extract yielded 3.8 g (22%) of α-naphthoic acid, the m.p. of which was 158° after recrystallization from water.

0.2081 g substance: consumed in titration 24.01 ml 0.05 $\underline{N}$ NaOH. Found: M 173.3. $C_{11}H_8O_2$. Computed: M 172.

2. Oxidation of the methyl ester of α-naphthylacetic acid. A mixture of 10 g of the methyl ester of naphthylacetic acid and 5.6 g of freshly sublimed selenium was heated for 1.5 hours over a metallic bath, the temperature of which was 190°. After this time had elapsed and the mixture had cooled, the reaction product was dissolved in ether, and the selenium was filtered out. Its yield totaled 3.6 g (92.3%). The ether solution was washed with a soda solution and with water. After it had been desiccated, the ether was driven off, and the residue was distilled in vacuum; this yielded 7.8 g (68%) of a crystalline substance that boiled at 201-203° and 37 mm. Its m.p. was 73° after double recrystallization from petroleum ether. The picrate of the ester had a m.p. of 81°.

0.1946 g and 0.2362 g of the picrate: consumed in neutralizing the ammonia, 13.04 and 15.92 ml 0.1 $\underline{N}$ H_2SO_4. Found %: N 9.38, 9.43. $C_{18}H_{13}O_{10}N_3$. Computed %: N 9.48.

Acidification of the soda solution yielded about 1.2 g (14%) of α-naphthoic acid, the m.p. of which was 158° after crystallization from water.

3. Oxidation of the ethyl ester of α-naphthylacetic acid. 16 g of the ethyl ester of naphthylacetic acid was oxidized at 200-210° by 8.4 g of selenium dioxide under the conditions described under Experiment 2. Appropriate treatment yielded 5.5 g (93%) of selenium, 1.8 g (14%) of naphthoic acid, and 12.8 g (72%) of the ethyl ester of naphthoylformic acid (b.p. 210-212° at 20 mm). The ester was identified by preparing its picrate, which had a m.p. of 76-76.5°, which conforms to the melting point given in the literature, [9].

SUMMARY

A study has been made of the oxidation of α-naphthylacetonitrile and of the esters of naphthylacetic acid by selenium dioxide. It has been shown that the oxidation of naphthylacetonitrile and of the esters of naphthylacetic acid

follow a common pattern, the methylene group being converted into a carbonyl group.

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THE SYNTHESIS OF 1-METHYL-4-ALKYLCYCLOHEXEN-1-ONES-3

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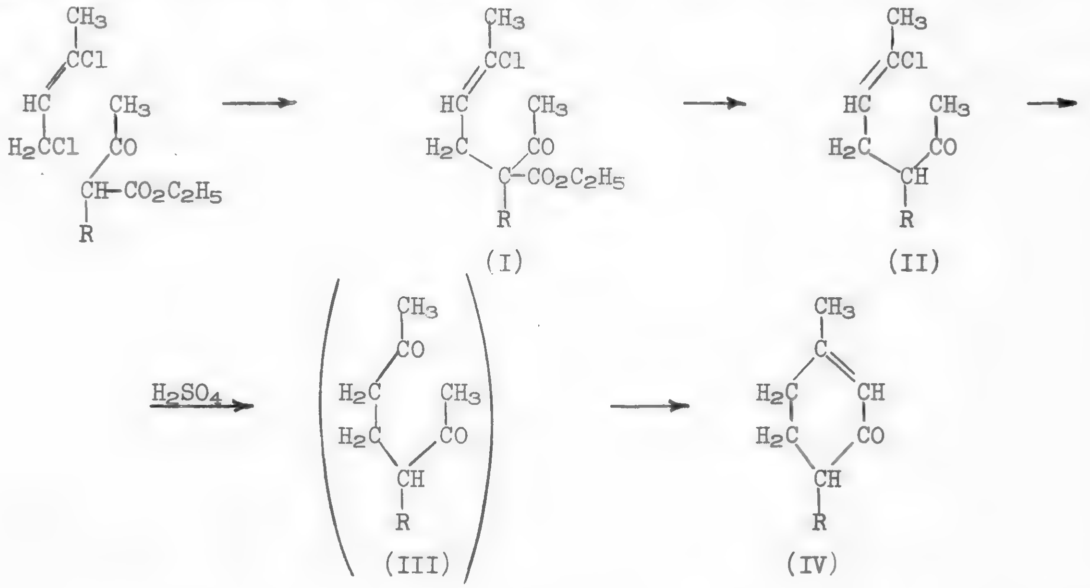
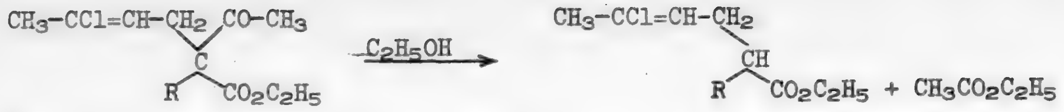
As we know, certain alkylated Δ^2-cyclohexenones have made their way into the pharmaceutical industry and into the manufacture of perfumes. Moreover, homologs of Δ^2-cyclohexenone are employed rather frequently as raw materials or intermediates in laboratory syntheses. That is why methods of synthesizing these ketones, the development of which goes back as far as the last quarter of the past century, still interest research workers. The commonest and most frequently employed methods of producing homologs of Δ^2-cyclohexenone are based upon cyclizing 1,5-diketones [1]. Methods elaborated by different authors differ only in the ways used to secure the intermediate 1,5-diketo derivatives.

It has been shown previously that homologs of Δ^2-cyclohexenone can be prepared by hydrolyzing the respective unsaturated chloroketones with sulfuric acid. It was found [2] that 6-chlorohepten-5-one-2 (II, R = H), synthesized by G.I. Isagulyants [3] by condensing 1,3-dichlorobutene-2 with acetoacetic ester, followed by ketonic cleavage of the substituted acetoacetic ester (I, R = H), is hydrolyzed and cyclized by concentrated sulfuric acid, yielding 1-methylcyclohexen-1-one-3 (IV, R = H).



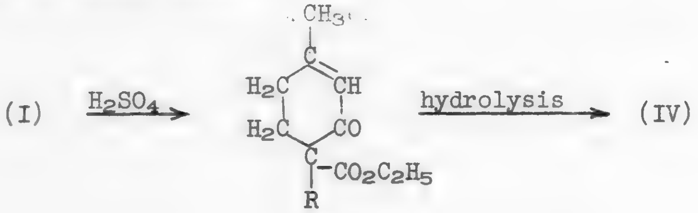
1,4-Dimethylcyclohexen-1-one-3 (IV, R = CH_3), was prepared in the same way from methyl-(γ-chlorocrotyl)-acetoacetic ester (I, R = CH_3). Efforts to synthesize other 1-methyl-4-alkylcyclohexen-1-ones-3 in the same manner indicated that disubstituted acetoacetic esters (I, R = H, CH_3) are quite unstable, readily hydrolyzing when heated in a weakly alkaline medium, even at the instant of their formation:



When no excess alkali is present, the resulting disubstituted acetoacetic esters suffer no change.

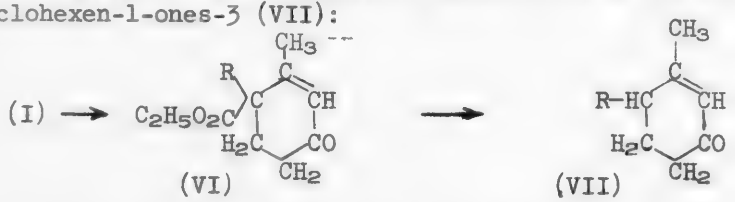
In the synthesis of 1-methyl-4-isopropylcyclohexenone the 1,3-dichlorobutene-2 was condensed with isopropylacetoacetic ester at room temperature in order to avoid alcoholysis, so that the reaction was not complete, the yield of isopropyl-(γ-chlorocrotyl)-acetoacetic ester being 27.5% of the theoretical. In preparing other ketones, however, we found that no alcoholysis occurs if no excess alkali is present, even at a higher temperature, so that we were able to secure the other disubstituted acetoacetic esters with high yields.

The marked tendency of these esters toward acid cleavage prevented the securing of alkylchloroheptenones (II) from them, so that the plan of synthesis was modified to have the alkyl-(γ-chlorocrotyl)-acetoacetic esters hydrolyzed and cyclized by sulfuric acid directly. The resultant cyclic ketonic esters (V) are partially hydrolyzed by the sulfuric acid, so that we get the esters together with a certain amount of the respective cyclic ketones, which are separated by fractionating the mixtures. The cyclic ketonic esters are then hydrolyzed by boiling with an alcoholic alkali:



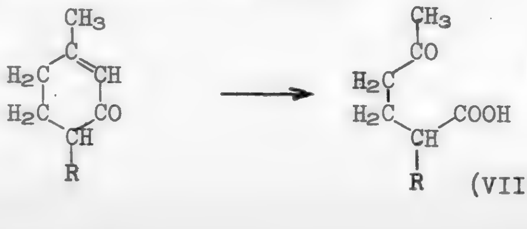
(V)

The asymmetrical 1,5-diketonic esters, which yield disubstituted acetoacetic esters when hydrolyzed by sulfuric acid, can be cyclized at the expense of two carbonyl groups. The formation of 1-methyl-6-alkyl-6-carbethoxycyclohexen-1-ones-3 (VI) was not impossible, hydrolysis of the latter yielding 1-methyl-6-alkylcyclohexen-1-ones-3 (VII):



(VI) (VII)

The absence of a substituent at the α-position to the carbonyl group formed during hydrolysis at the expense of the chlorine atom sterically promotes an intramolecular aldol condensation at the expense of this carbonyl group; we therefore had to expect that the only compounds formed or the principal ones would be cyclic ketonic esters and ketones with the hydrocarbon radicals at the 1 and 4 positions. The structure of the ketones was determined by oxidation with potassium permanganate. In this oxidation 1-methyl-4 alkyl-cyclohexen-1-ones-3 ought to yield α-alkyl-γ-acetylbutyric acids (VIII)



(VIII)

whereas the oxidation products of 1-methyl-6-alkylcyclohexen-1-ones-3 (VII) would be the respective γ-alkyl-γ-acetylbutyric acids. The oxidation products of all four ketones proved to be the corresponding α-alkyl-γ-acetylbutyric acids, which were identified as their semicarbazones. Thus, of the two possible isomers, only 1-methyl-4-alkylcyclohexen-1-ones-3 were formed in all the instances we investigated.

Of the ketones synthesized, the most interesting is 1-methyl-4-isopropylcyclohexen-1-one-3, which is the d,l form of the natural ketone piperitone, the fragrant base of several eucalyptus oils, which has been employed in industry owing to the readiness with which it can be converted into thymol, menthol, and menthone.

Synthetic piperitone was first prepared by Walker [5] by a method similar to the one described in the present paper, viz.: condensing methyl β-chloroethyl ketone with isopropylacetoacetic ester, cyclizing the condensation product, and saponifying the cyclic ketonic ester.

Piperitone has also been prepared [6] by brominating 1-methyl-4-isopropyl-4-carbethoxycyclohexanone-3, splitting out hydrogen bromide from the resulting α-bromoketone by heating the latter to 150-160° with tertiary amines, and saponifying the unsaturated ketonic ester.

Lastly, Birch [7] secured a negligible yield of piperitone by reducing 5-methyl-2-isopropylanisole with sodium and alcohol in liquid ammonia, and then hydrolyzing and isomerizing the 1,4-dihydro derivative resulting from the reduction.

In view of the fact that 1,3-dichlorobutene-2, which we have used as our initial material, is produced in large quantities as a waste product in one of our chemical industries, the method described in the present paper must be considered the most convenient and cheapest process for the synthetic production of d,l-piperitone.

1-Methyl-4-n-butyl- and 1-methyl-4-isoamylcyclohexen-1-ones-3 are likewise fragrant, their odors differing somewhat from that of piperitone. The high-boiling 1-methyl-4-benzylcyclohexen-1-one-3 has no odor at all.

EXPERIMENTAL

1-Methyl-4-isopropylcyclohexen-1-one-3 (d,l-Piperitone)

Isopropyl-(γ-chlorocrotyl)-acetoacetic ester (I, R = iso-C_3H_7). 85.6 g of freshly distilled 1,3-dichlorobutene-2 was gradually added to a solution of the sodium derivative of isopropylacetoacetic ester, prepared from 80 g of that ester, 10 g of sodium, and 114 g of absolute alcohol with stirring and water-cooling. The reaction mixture was allowed to stand for 3 days at room temperature, after which water acidulated with hydrochloric acid was added (the precipitate dissolves completely), the resultant product was dissolved in benzene, and the benzene solution was washed with water and desiccated with anhydrous sodium sulfate. The solvent was driven off, and the product was distilled in vacuum. This yielded 32 g (27.75% of the theoretical quantity) of a substance that had a b.p. of 124-127° at 5 mm.

$d_4^{21.75}$ 1.0715; $n_D^{21.75}$ 1.4720; MR_D 68.07; computed 68.30.

0.1820 g substance: 0.0990 g AgCl. 0.1642 g substance: 0.0914 g AgCl. Found %: Cl 13.46, 13.78. $C_{13}H_{21}O_3Cl$. Computed %: Cl 13.68.

1-Methyl-4-isopropyl-4-carbethoxycyclohexen-1-one-3 (V, R = iso-C_3H_7). 9.6 g of sulfuric acid, sp. gr. 1.78, was added, with stirring and chilling with ice, to 10.1 g of isopropyl-(γ-chlorocrotyl)-acetoacetic ester. The reaction mixture was allowed to stand for two days, after which 15.4 ml of water and 15.7 g of anhydrous soda were added. The reaction product was extracted with ether; the ether solution was washed with water and desiccated with anhydrous sodium sulfate. The ether was driven off, and the product was fractionated in vacuum. Refractionation yielded 0.43 g of a fraction that boiled at 102-104° and 9 mm, consisting chiefly of 1-methyl-4-isopropylcyclohexenone, 0.85 g of an intermediate fraction, and 5.48 g (63.1% of the theoretical) of the principal product, a colorless oil with a b.p. of 141-144° at 9 mm. 1-Methyl-4-isopropyl-4-carbethoxycyclohexen-1-one-3 had been described previously by Walker [5]. The product we synthesized had the following properties:

$d_4^{20.25}$ 1.0398; $n_D^{20.25}$1.4838; MR_D 61.61; computed 61.23; EM_D 0.38.

0.1028 g substance: 0.2628 g CO_2; 0.0808 g H_2O. Found %: C 69.72; H 8.73. $C_{13}H_{20}O_3$. Computed %: C 69.64; H 8.93.

1-Methyl-4-isopropylcyclohexen-1-one-3 (IV, R = iso-C_3H_7). A mixture of 8.79 g of the ester (V, R = iso-C_3H_7) with a solution of 6.79 g of potassium hydroxide in 35 ml of methanol was boiled for 12 hours, and then dilute hydrochloric acid was added until its reaction was acid. The product was extracted with benzene, and the benzene solution was washed with water and desiccated with anhydrous sodium sulfate. The benzene was driven off, and the product was double distilled in vacuum. This yielded 3.72 g (62.42% of the theoretical) of a colorless oil with the odor of mint, which had a b.p. of 111-114° at 14 mm.

d_4^{20} 0.9415; n_D^{20} 1.4841; MR_D 46.17; computed 45.72; EM_D 0.45.

Oxime. A water-alcohol solution of 0.92 g of hydroxylamine hydrochloride, 2.16 g of sodium acetate, and 1.82 g of the ketone was boiled for 6 hours, after which the mixture was diluted with water and treated several times with small quantities of ether. The oxime was extracted from the ether solution with dilute sulfuric acid. Adding an alkali to the sulfuric-acid solution yielded an oil that soon crystallized. The colorless crystals had a m.p. of 117-118° after recrystallization from alcohol (the α-oxime of d,l-piperitone).

Oxidation. A solution of 3.45 g of potassium permanganate and 0.17 g of potassium hydroxide in 82 ml of water was gradually added, with stirring and chilling with ice water, to 1.28 g of the ketone. The reaction mixture was allowed to stand at room temperature until it was decolorized (2 days), after which it was filtered. The filtrate was evaporated to the consistency of syrup, the residue being acidified with hydrochloric acid and the product triply extracted with ether. Driving off the ether left behind an oil, to which a solution of semicarbazide and sodium acetate was added. The colorless crystals of the semicarbazone, formed after prolonged standing and double crystallization from aqueous alcohol, had a m.p. of 156-157° (the semicarbazone of α-isopropyl-γ-acetylbutyric acid).

1-Methyl-4-n-butylcyclohexen-1-one-3

n-Butyl-(γ-chlorocrotyl)-acetoacetic ester (I, R = n-C_4H_9). This was prepared by a method resembling that for isopropyl-(γ-chlorocrotyl)-acetoacetic ester: by condensing 82.42 g of 1,3-dichlorobutene-2 with the sodium derivative of butylacetoacetic ester, prepared from 81.76 g of butylacetoacetic ester, 9.45 g of sodium, and 106.8 g of absolute alcohol, the only difference being that in this case the reaction mixture was allowed to stand overnight at room temperature, after which it was heated to 50-60° for 5-6 hours. This yielded 87.51 g (72.53% of the theoretical) of a colorless substance with a b.p. of 107-108° at 2 mm.

d_4^{18} 1.0396; n_D^{18} 1.4658; MR_D 73.10; computed 72.92.

0.1122 g substance: 0.0582 g AgCl; 0.1158 g substance: 0.0604 g AgCl. Found %: Cl 12.84, 12.91. $C_{14}H_{23}O_3Cl$. Computed %: Cl 12.93.

1-Methyl-4-n-butyl-4-carbethoxycyclohexen-1-one-3 (V, R = n-C_4H_9) 39.34 g of butyl-(γ-chlorocrotyl)-acetoacetic ester was hydrolyzed with 35 ml of sulfuric acid, sp. gr. 1.78. The reaction was similar to the hydrolysis of isopropyl-(γ-chlorocrotyl)-acetoacetic ester. After the solvent had been driven off from the ether solution of the reaction product, the residue was doubly fractionated in vacuum. This yielded 1.58 g of a fraction with a b.p. of 96-98° at 3 mm, consisting chiefly of the ketone, 4.3 g of an intermediate fraction, and 21.4 g (62.76% of the theoretical) of the principal product as a colorless liquid with a b.p. of 111.5-112.5° at 2 mm.

d_4^{23} 1.0155; n_D^{23} 1.4780; MR_D 66.34; computed 65.85; EM_D 0.49.

0.1016 g substance: 0.2606 g CO_2; 0.0838 g H_2O. 0.1216 g substance: 0.3131 g CO_2; 0.1046 g H_2O. Found %: C 69.95, 70.22; H 9.17, 9.55. $C_{14}H_{22}O_3$. Computed %: C 70.59; H 9.24.

1-Methyl-4-n-butylcyclohexen-1-one-3 (IV, R = n-C_4H_9). This was synthesized like the d,l-piperitone, by hydrolyzing 40.02 g of the cyclic ketonic ester (V, R = n-C_4H_9) with 28.31 g of potassium hydroxide dissolved in 142 ml of methanol. Double distillation in vacuum yielded 13.59 g (47.27%. of the theoretical) of a fragrant, colorless liquid with a b.p. of 95-96° at 4 mm.

$d_4^{20.5}$ 0.9314; $n_D^{20.5}$ 1.4790; MR_D 50.54; computed 50.34.
0.1102 g substance: 0.3212 g CO_2; 0.1118 g H_2O. Computed %: C 79.57; H 11.27. $C_{11}H_{18}O$. Computed %: C 79.52; H 10.84.

Semicarbazone. This was prepared by allowing a mixture of the ketone to stand for a long time with a solution of semicarbazide hydrochloride and sodium acetate. It had a m.p. of 190-192° after double recrystallization from alcohol.

Oxidation. 3.39 g of the ketone was oxidized by a solution of 8.36 g of potassium permanganate and 0.4 g of potassium hydroxide in 199 ml of water. Oxidation was similar to that of the d,l-piperitone. The semicarbazone of the oxidation product had a m.p. of 142-144° after recrystallization from water. A test sample mixed with the known semicarbazone of α-n-butyl-γ-acetylbutyric acid [8], which had a m.p. of 139-140°, exhibited no depression (m.p. 140-142°).

1-Methyl-4-isoamylcyclohexen-1-one-3

Isoamyl-(γ-chlorocrotyl)-acetoacetic ester (I, R = iso-C_5H_{11}). This was prepared by a method similar to that used in preparing butyl-(γ-chlorocrotyl)-acetoacetic ester: by condensing 56.4 g of 1,3-dichlorobutene-2 with the sodium derivative of isoamylacetoacetic ester, prepared from 60 g of isoamylacetoacetic ester, 6.45 g of sodium, and 73 g of absolute alcohol. This yielded 46.07 g (53.23% of the theoretical) of a colorless substance with a b.p. of 116-118° at 2 mm.

$d_4^{21.3}$ 1.0262; $n_D^{21.3}$ 1.4642; MR_D 77.60; computed 77.54.

0.1152 g substance: 0.0580 g AgCl. 0.1070 g substance: 0.0530 g AgCl. Found %: Cl 12.45, 12.25. $C_{15}H_{25}O_3Cl$. Computed %: Cl 12.30.

1-Methyl-4-isoamyl-4-carbethoxycyclohexen-1-one-3 (V, R = iso-C_5H_{11}). This was prepared like the cyclic ketonic esters described previously: by the acid hydrolysis and cyclization of 41.31 g of isoamyl-(γ-chlorocrotyl)-acetoacetic ester with 35 ml of sulfuric acid. Triple fractionation of the reaction products in vacuum yielded 1.45 g of a fraction with a b.p. of 86-88° at 2 mm, consisting of the corresponding ketone (IV, R = iso-C_5H_{11}), 3.9 g of an intermediate fraction, and 20.04 g (55.54% of the theoretical) of the principal product, a colorless liquid with a b.p. of 112-115° at 2 mm.

$d_4^{24.5}$ 1.0015; $n_D^{24.5}$ 1.4768; MR_D 71.07; computed 70.47; EM_D 0.60.

3.200 mg substance: 8.315 mg CO_2; 2.726 mg H_2O. 3.484 mg substance: 9.075 mg CO_2; 3.010 mg H_2O. Found %: C 70.91, 71.08; H 9.53, 9.67. $C_{15}H_{24}O_3$. Computed %: C 71.43; H 9.52.

1-Methyl-4-isoamylcyclohexen-1-one-3 (IV, R = iso-C_5H_{11}). This was produced by a method similar to that used for the cyclic ketones described above: by hydrolyzing 18.09 g of the ester (V, R = iso-C_5H_{11}) with a solution of 12.07 g of potassium hydroxide in 60 ml of ethyl alcohol. Double distillation yielded 5.10 g (39.47% of the theoretical) of a fragrant, colorless liquid with a b.p. of 84-86° at 2 mm.

d_4^{19} 0.9196; n_D^{19} 1.4808; MR_D 55.68; computed 54.96; EM_D 0.72.

0.1318 g substance: 0.3841 g CO_2; 0.1350 g H_2O. Found %: C 79.47; H 11.38. $C_{12}H_{20}O$. Computed %: C 80.00; H 11.11.

Semicarbazone. The semicarbazone fused at 181-183° after double recrystallization from alcohol.

Oxidation. 0.26 g of the ketone was oxidized by a solution of 6 g of potassium permanganate and 0.29 g of potassium hydroxide in 142.5 ml of water. The semicarbazone of the oxidation product had a m.p. of 150-152° after double recrystallization from water. A test sample, mixed with the semicarbazone of α-isoamyl-γ-acetylbutyric acid [8] with a m.p. of 152-154°, exhibited no depression (152-153°).

1-Methyl-4-benzylcyclohexen-1-one-3

Benzyl-(γ-chlorocrotyl)-acetoacetic ester (I, R = $C_6H_5-CH_2$). This was prepared like butyl-(γ-chlorocrotyl)-acetoacetic ester: by condensing 47 g of 1,3-di-chlorobutene-2 with the sodium derivative of benzylacetoacetic ester, prepared from 55 g of benzylacetoacetic ester, 5.37 g of sodium, and 61 g of absolute alcohol. This yielded 56.46 g (73.21% of the theoretical) of a colorless substance that had a b.p. of 146-148° at 2 mm.

$d_4^{16.5}$ 1.1234; $n_D^{16.5}$ 1.5202; MR_D 83.51; computed 83.17.

0.1176 g substance: 0.0540 g AgCl. 0.1166 g substance: 0.0536 g AgCl. Found %: Cl 11.37, 11.38. $C_{17}H_{21}O_3Cl$. Computed %: Cl 11.51.

1-Methyl-4-benzyl-4-carbethoxycyclohexen-1-one-3 (V, R = $C_6H_5-CH_2$). 53.84 g of benzyl-(γ-chlorocrotyl)-acetoacetic ester was hydrolyzed and cyclized by reacting it with 42.6 ml of sulfuric acid, sp. gr. 1.78. Fractionation of the reaction products yielded 2.1 g of a fraction with a b.p. of 128-130° at 2 mm, consisting mainly of a cyclic ketone (IV, R = $C_6H_5-CH_2$), 4.5 g of an intermediate fraction, and 29.18 g (61.6% of the theoretical) of the cyclic ketonic ester as a colorless liquid that crystallized and had a m.p. of 43-44° after recrystallization from alcohol.

0.1127 g substance: 0.3097 g CO_2; 0.0769 g H_2O. 0.1031 g substance: 0.2828 g CO_2; 0.0701 g H_2O. Found %: C 74.94, 74.80; H 7.58, 7.55. $C_{17}H_{20}O_3$. Computed %: C 75.00; H 7.35.

1-Methyl-4-benzylcyclohexen-1-one-3 (IV, R = $C_6H_5-CH_2$). This was prepared like the other unsaturated cyclic ketones: by saponifying 24.28 g of the ester (V, R = $C_6H_5-CH_2$) with a solution of 15 g of potassium hydroxide in 60 ml of methanol. This yielded 13.22 g (74.06% of the theoretical) of a colorless oil with a b.p. of 125-127° at 2 mm.

$d_4^{27.75}$ 1.0367; $n_D^{27.75}$ 1.5511; MR_D 60.40; computed 60.80.

0.1114 g substance: 0.3406 g CO_2; 0.0798 g H_2O. 0.1150 g substance: 0.3454 g CO_2; 0.0816 g H_2O. Found %: C 83.38, 83.36; H 7.96, 8.01. $C_{14}H_{16}O$. Computed %: C 84.00; H 8.00.

Semicarbazone. The semicarbazone had a m.p. of 189-190° after double recrystallization from alcohol.

Oxidation. 4.43 g of the ketone was oxidized with a solution of 9.07 g of potassium permanganate and 0.44 g of potassium hydroxide in 215 ml of water. Upon distillation of the oxidation product in vacuum there first sublimed a small amount of a colorless substance with a m.p. of 120-121°. A test sample, mixed with benzoic acid, exhibited no depression of the melting point. Then a thick oil that crystallized upon standing distilled at 180-185° and 3 mm. The squeezed-out crystals had a m.p. of 63-65°. A test sample, mixed with α-benzyl-γ-acetylbutyric acid [8] that had a m.p. of 63-64°, fused at 63-65°.

SUMMARY

1. It has been shown that 1-methyl-4-alkylcyclohexen-1-ones-3 can be prepared by a sulfuric-acid hydrolysis and cyclization of alkyl-(γ-chlorocrotyl)-acetoacetic esters, followed by hydrolysis and decarboxylation of the resultant cyclic β-ketonic esters. The yield of the ketones ranges from 40 to 74% of the theoretical.

2. It has been shown that in all the instances we have investigated, of the two possible isomers, those isomers are formed that have alkyl groups at the 1 and 4 positions.

3. In addition to 1-methyl-4-n-butyl-, 1-methyl-4-isoamyl-, and 1-methyl-4-benzylcyclohexenones, which have been synthesized and described for the first time, the specified method has been used to synthesize 1-methyl-4-isopropylcyclohexen-1-one-3, which is the d,l-form of the natural ketone piperitone.

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SULFONATION AND SULFO ACIDS OF ACIDOPHOBIC COMPOUNDS

XV. SULFONATION OF DIENE HYDROCARBONS WITH CONJUGATED DOUBLE BONDS

A. P. Terentyev and A. V. Dombrovsky

In our previous reports [1] we demonstrated that pyridine sulfotrioxide could be used to sulfonate with satisfactory yields such readily-tarring diene hydrocarbons as α-phenylbutadiene and cyclopentadiene. Continuing our investigation, we tested a number of the simplest dienes with conjugated double bonds.

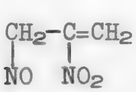
We found that pyridine sulfotrioxide is a quite satisfactory sulfonating agent for these compounds. Sulfonation of divinyl, isoprene, 2,3-dimethylbutadiene, and other homologs of divinyl results in the formation of sulfo acids with the sulfo group attached at the double bond, i.e., substitution occurs in the vinyl position.

Examples of the substitution of the sulfo group for hydrogen atoms at the double bond are somewhat surprising, at any rate rather uncommon. We are accustomed to associate reactions involving the substitution of various groups for hydrogen atoms with saturated or aromatic compounds. In the olefins, and even more so in the diolefins, these reactions are known as rare and solitary exceptions. Still, if we make a careful survey of the factual data, such reactions are not anomalies. Very frequently, substitution reactions occur in the case of the diolefins as side processes accompanying addition reactions, though at times substitution is the principal process, as at high temperature, for example, especially in the case of hydrocarbons with activated double bonds. In the aromatic hydrocarbons, on the other hand, addition products are often observed, as we know, alongside the usual direct substitution reactions. The former are frequently unstable at high temperature. This leads may authors (Hollemann, K. Meyer, Wieland, etc.) to regard the addition products as intermediates in typical substitution reactions of aromatic compounds.

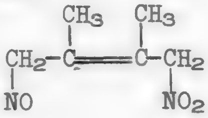
Hence, the substitution reactions of the olefins relate them to the typical aromatic compounds. A study of similar transformations and of the order in which the substituents enter was not without interest. We shall consider only the substitution of vinylic atoms for hydrogen in olefins.

In the halogenation of the dienes this sort of metalepsy has been observed only in isolated cases as a side reaction. Jones and Williams [2] passed chlorine through a chilled solution of isoprene in carbon tetrachloride and observed the evolution of hydrogen chloride. They recovered 1-chloro-2-methylbutadiene-1,3. According to V.I.Esafov [3], 59% of conjugated dienes dissolved in carbon tetrachloride react, with substitution, whereas only 2-3% of dienes with isolated double bonds react. Unfortunately, this author did not establish the structure of the substance he had prepared, so that his data provides no information on the point of entry of the halogen atom into the diene molecule. It is worthy of note that when natural isoprene rubber is chlorinated in a carbon tetrachloride solution, the substitution reaction is 82% of the theoretical [4].

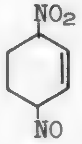
Diene hydrocarbons react energetically with nitrating agents. N.Ya.Demyanov and A.A.Ivanov [5], as well as A.S.Onishchenko [6], have shown that allene, 2,3-dimethylbutadiene, and cyclohexadiene-1,3 add N_2O_3 at the double bond, yielding the respective nitrosates:

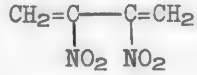


$\underset{NO}{CH_2}-\underset{NO_2}{C}=CH_2$

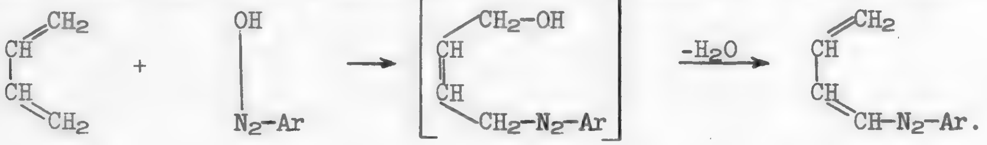


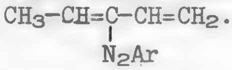
$\underset{NO}{CH_2}-\overset{CH_3}{C}=\overset{CH_3}{C}-\underset{NO_2}{CH_2}$

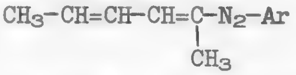


Demyanov concluded that no more than two NO_2 groups or one molecule of N_2O_3 is ever added to a diene molecule. No one has ever observed the replacement of hydrogen by nitro groups in dienes as yet. In this regard, it is not without interest to quote a statement by I.I.Ostromyslensky, who wrote in 1915: "I have reason to believe that erythrene, nitrated under suitable conditions, would yield the dinitro compound  $CH_2=\underset{NO_2}{C}-\underset{NO_2}{C}=CH_2$, which is most likely a very close analog of trinitrobenzene" [7].

In 1919 K. Meyer [8] prepared well-crystallized azo compounds of divinyl, isoprene, piperylene, and 2,3-dimethylbutadiene. According to Meyer, a diazo compound is added as a syn-diazohydrate at the double bond, forming the initial product, which then loses a molecule of water, yielding the azo compound:



Meyer believed that the ability of unsaturated compounds to react with diazo compounds was governed by the activity of the carbon-carbon double bond. This activity is increased by the effects of certain substituent groups at the double bond. An azo group replaces the hydrogen atom at the double bond that is in the β-position to a methyl group. That is why Meyer considered the structure of the coupling product of piperylene to be  $CH_3-CH=\underset{N_2Ar}{C}-CH=CH_2$. The conclusions reached by B.A.Arbuzov and S.Rafikov [9], who assumed that replacement by an azo group occurs at the end of the conjugated system, are more logical and convincing. They actually demonstrated that the products of the azo coupling of piperylene and hexadiene-2,4 had the following structures, respectively:

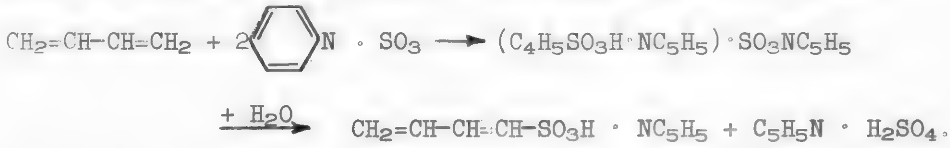
$CH_3-CH=CH-CH=CH-N_2-Ar$ and  $CH_3-CH=CH-CH=\underset{CH_3}{C}-N_2-Ar$.

A.P.Terentyev [10] and his co-workers continued this research on the azo coupling reaction with mono- and diolefins. They found that even such dienes as phenylbutadiene entered into an azo coupling reaction. On the basis of these investigations they worked out a method for the qualitative and quantitative determination of conjugated dienes [11].

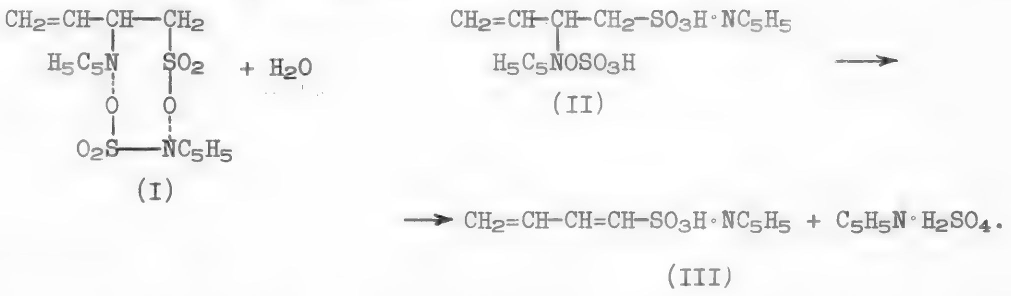
As for the sulfonation of divinyl and its homologs, there is nothing in the literature on this subject. As we know, the direct action of H_2SO_4, $ClSO_3H$, or SO_3 on conjugated dienes causes rapid polymerization and tarring. It has been found that 68-70% sulfuric acid absorbs divinyl fairly vigorously at a constant rate. The polymerization and tarring involved occur with such ease that drops of oil are formed on the surface of the acid [12]. Even dioxane sulfotrioxide, a milder sulfonating agent, employed by Suter and his co-workers [13] to introduce the sulfo group into several mono-olefins, proved to be unsuitable for conjugated dienes, according to our observations. Dioxane sulfotrioxide causes pronounced darkening and tarring of divinyl, isoprene, 2,3-dimethylbutadiene, and other dienes, even at low temperatures and in dilute solutions. Hence, none of the methods described in the literature yields satisfactory results when used with conjugated dienes.

Our method, after prolonged development, has made it possible to produce satisfactory yields of sulfo acids and their derivatives of unsaturated hydrocarbons with conjugated double bonds. We have sulfonated butadiene-1,3 and several of its homologs with pyridine sulfotrioxide.

Butadiene-1,3. We sulfonated divinyl by heating it to 100-110° for 8-10 hours with pyridine sulfotrioxide in dichloroethane in a stainless-steel autoclave. Treating the mass with concentrated ammonia and a baryta solution yielded the barium salt of α-divinylsulfo acid $(CH_2{=}CH{-}CH{=}CH{-}SO_3)_2Ba$ (butadiene-1,3-sulfonic-1 acid), the yield being 77%, based on the divinyl. The highest yields of divinylsulfo acid are secured by using two mols (or slightly more) of pyridine sulfotrioxide per mol of divinyl. This suggested that one molecule of divinyl reacts with two molecules of pyridine sulfotrioxide. We checked this by heating pyridine sulfotrioxide to 100-110° with a large excess of divinyl until all the sulfonating agent had reacted. The primary product was isolated by treating the sulfo mass with absolute ether. Determination of the carbon, hydrogen, and nitrogen indicated that two mols of pyridine sulfotrioxide combines with one mol of divinyl. Boiling the primary product in water for a short while splits off half of the added sulfur trioxide as a sulfate ion. Hence, the reaction between pyridine sulfotrioxide and divinyl may be represented as follows:


CH2=CH–CH=CH2 + 2 N · SO3 → (C4H5SO3H·NC5H5)·SO3NC5H5
+ H2O → CH2=CH–CH=CH–SO3H · NC5H5 + C5H5N · H2SO4.

The structure of the primary product may be represented by Formula (I). Then hydrolysis proceeds in accordance with:



This explains the rather difficult elimination of part of the pyridine when the salt is treated with baryta.

α-Divinylsulfo acid is a strong acid that is quite stable in solutions. 50% solutions of this acid have been kept for a year and a half without perceptible change. The acid darkens when an effort is made to secure it in an anhydrous state by evaporating its solution over a water bath or in a vacuum desiccator. The thick mass that results deliquesces in the air and does not crystallize even after standing for a long time in a vacuum desiccator above sulfuric acid. The acid is freely soluble in water, in methanol, and in ethyl alcohol. The Ba, Na, K, Ca, and Pb salts of α-divinylsulfo acid are white crystalline substances, which are shown to be salts of a monosulfo acid upon analysis. They are all freely soluble in water and insoluble in organic solvents. The salts of nitrogen bases (ammonium, diethylamine, pyridine, and piperidine) dissolve in methanol and ethyl alcohol. These salts have a viscous consistency, and we were unable to secure then in a crystalline state. When the barium salt is heated with dilute acids for two hours, 20% hydrolysis occurs. Divinylsulfo acid and its salts possess obvious unsaturated properties. Their aqueous solutions decolorize permanganate and bromine water instantaneously in the cold.

Proof of the structure of the divinylsulfo acid. The structure of the synthesized sulfo acid might be proved by reducing its derivatives to butanesulfonic acids and then identifying their derivatives, which have been described in the literature. We were unable, however, to reduce the divinylsulfo acid completely. The usual method of reduction with hydrogen iodide in the presence of red phosphorus could not be used, since the divinylsulfo acid is completely decomposed at high temperature (170°) in a strongly acid medium, a sulfate ion being evolved and a carbonlike mass being formed. Nor was reduction of the sulfo acid with sodium amalgam, which can be successfully employed to reduce vinylacrylic acid to β-ethylidenepropionic and valeric [14] acids, of any use in our case. We succeeded in hydrogenating the aqueous Na, K, and Ba salts of the divinylsulfo acid by using Raney nickel. This resulted in the addition of only two atoms of hydrogen, the end product being butene-1-sulfonic-1 acid, $CH_3-CH_2-CH=CH-SO_3H$.

The salts of this acid are white crystalline substances that are freely soluble in water. They also decolorize permanganate and bromine water. Preparing products of incomplete hydrogenation enabled us to determine the structure of the original divinylsulfo acid. When the potassium salt of the divinylsulfo acid was oxidized with potassium permanganate, the sulfo group was split off as a sulfate ion. The conditions used for this reaction were like those used in oxidizing propylideneacetic acid, $CH_3-CH_2-CH=CH-COOH$ [15], this latter acid being ruptured at the double bond, giving rise to propionic acid. Oxidation of our partially hydrogenated divinylsulfo acid yielded propionic acid, identified as its silver salt. This is enough to fix the structure of the dihydro acid and, hence, of the original divinylsulfo acid as butadiene-1,3-sulfonic-1 acid.

An addition reaction to the divinylsulfo acid is very difficult, despite its having conjugated double bonds. When aqueous solutions of its salts are hydrogenated, even with a considerable excess of nickel (10 g of nickel per 40 ml of a 10% solution), no more than two atoms of hydrogen are added. No hydrohalic acids can be added, inasmuch as heating with acids results in hydrolysis and decomposition. Nor does addition occur when the divinylsulfo acid and its salts are heated with anhydrous and water-alcoholic solutions of diethylamine and piperidine. Apparently, the sulfo group strongly passivates the divinyl molecule. Aqueous solutions of the divinylsulfo acid decolorize bromine water, one mol of bromine requiring one mol of the sulfo acid. This does not result in addition, however, one hydrogen atom being replaced by bromine. Experiment has shown that a mol of hydrogen bromide is evolved for every molecule of bromine entering into the reaction. There are cases described in the literature in which the hydrogen at the double bond, in the α-position to the sulfo group, is replaced by bromine. Kohler [16] made a study of the properties of ethylenesulfo acid, $CH_2=CH-SO_3H$, and found that its aqueous solutions react readily with bromine, evolving hydrogen bromide and yielding a bromine-substituted sulfo acid, $CH_2=CBrSO_3H$. Ingold and Smith [17] have shown that when this acid is reacted with iodine chloride, its α-hydrogen atom is replaced by chlorine, $CH_2{=}CClSO_3H$ being formed. The same properties are displayed by ω-styrenesulfo acid and its salts, [18,19], which yield $C_6H_5{-}CH{=}CBrSO_3H$ when reacted with bromine, whereas $C_6H_5{-}CH{=}\underset{\underset{CH_3}{|}}{C}{-}SO_3H$ [20] does not react with bromine under similar conditions, inasmuch as it has no hydrogen atom in the α-position.

The foregoing justifies us in assuming that the reaction of the divinylsulfo acid with bromine is similar, i.e., the hydrogen atom in the α-position is replaced by a sulfo group:

$$CH_2{=}CH{-}CH{=}CH{-}SO_3H + BR_2 \longrightarrow CH_2{=}CH{-}CH{=}CBrSO_3H + HBr.$$

The composition of the barium salt was that of a monobromo-substituted divinylsulfo acid. All efforts to add bromine to the divinylsulfo acid at the double bonds by reacting the acid with bromine in methanol, glacial acetic acid, acetic anhydride, or even benzoyl peroxide were fruitless.

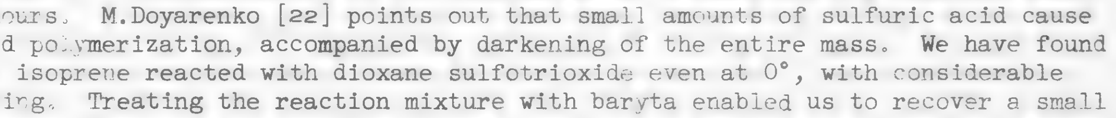
Derivatives of the divinylsulfo acid. The acid chloride of the divinylsulfo acid is prepared by treating the sodium or potassium salt with an excess of phosphorus pentachloride. It has a peculiar odor and is stable only in solutions of carbon tetrachloride, benzene, or ether. Water quickly causes the acid chloride to undergo a change, converting it into a completely inert solid, apparently a polymer.

Anilide of the divinylsulfo acid. This is a red crystalline substance with a m.p. of 83°. We were unable to prepare the amide of the divinylsulfo acid by reacting the acid chloride with ammonia or with ammonium carbonate.

Isoprene (2-methylbutadiene-1,3). Numerous papers have been devoted to a study of this compound. This hydrocarbon polymerizes with extraordinary ease. S.V.Lebedev has made a study of the kinetics of its polymerization [21]. He found that at 150° polymerization is 53% complete after 5 hours and 90% complete after 38 hours. M.Doyarenko [22] points out that small amounts of sulfuric acid cause rapid polymerization, accompanied by darkening of the entire mass. We have found that isoprene reacted with dioxane sulfotrioxide even at 0°, with considerable tarring. Treating the reaction mixture with baryta enabled us to recover a small amount of the barium salt of a sulfo acid. The minute quantities available made it impossible for us to determine its composition or structure. We sulfonated isoprene dissolved in dichloroethane by using pyridine sulfotrioxide at 100-110°. After the usual processing of the sulfo product, we isolated the barium salt of an unsaturated sulfo acid containing an appreciable quantity of a disulfo acid. Reprecipitation of the crude salt from methanol solutions yielded 58% of the theoretical quantity of the barium salt of an isoprenemonosulfo acid (2-methylbutadiene-1,3-sulfonic-1 acid):

$$[CH_2{=}CH{-}C(CH_3){=}CH{-}SO_3]_2Ba.$$

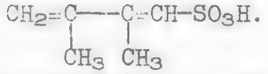
The Ba, Na, and K salts of the isoprenesulfo acid are crystalline substances that are quite stable in the solid state as well as in aqueous solutions. The barium salt of the isoprenesulfo acid was partially reduced above Raney's nickel to establish its structure. Oxidation of the resulting dihydro product yielded methyl ethyl ketone, which was identified as its p-nitrophenylhydrazone. This proved that the structure of the original sulfo acid was 2-methylbutadiene-1,3-sulfonic-1 acid:

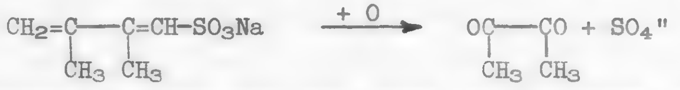


$$CH_2{=}CH{-}\overset{\overset{CH_3}{|}}{C}{=}CH{-}SO_3K \xrightarrow[(Ni)]{+H_2} CH_3{-}CH_2{-}\underset{\underset{CH_3}{|}}{C}{=}CH{-}SO_3K \xrightarrow{+\,O} C_2H_5COCH_3 + SO_4''$$

The properties of the isoprenesulfo acid and of its salts are like those of the divinylsulfo acid. Like the latter, it adds only two atoms of hydrogen in the presence of nickel. When reacted with oxidizing agents, it splits out the sulfo group as a sulfate ion. Reacting it with bromine results in a substitution reaction.

2,3-Dimethylbutadiene. This hydrocarbon was synthesized for the first time by N.Mariutsa, a pupil of Butlerov, by dehydrating dimethylisopropenylcarbinol [23]. Even at that time it was noted that the action of acid reagents, particularly sulfuric acid, at room temperature produces condensation of the hydrocarbon, accompanied by tarring. This readily changing diene is also polymerized when exposed to diffuse light in storage, heated, or kept for a long time above calcium chloride [24]. S.V.Lebedev investigated the nature and the rate of polymerization in the 50-150° range [25]. The only substitution reaction known for this hydrocarbon has been the azo coupling carried out by K. Meyer in 1919 [8].

Testing the action of pyridine sulfotrioxide on 2,3-dimethylbutadiene-1,3 at 100°, we found that this hydrocarbon does react, but that the reaction involves the formation of a large quantity of polymerization products in the shape of a spongy mass. This undesired process is suppressed, and the yield of the sulfo product is increased, by adding m-dinitrobenzene to the diene as a stabilizer and by performing the reaction in dichloroethane. Treating the sulfo mass in the usual manner yielded the barium salt of an unsaturated sulfo acid. Its barium content was higher than required for a monosulfo acid. This indicated the presence of products of more thoroughgoing sulfonation. Purification of the crude product by reprecipitation from aqueous solutions of methanol yielded the barium salt of 2,3-dimethylbutadiene-1,3-sulfonic-1 acid,  $CH_2{=}\underset{CH_3}{C}{-}\underset{CH_3}{C}{=}CH{-}SO_3H$. The barium salt, in turn, was used to secure the sodium and potassium salts. These are crystalline substances that are freely soluble in water. The acid and its salts are oxidized by permanganate, sulfur being split out as the sulfate ion. Its reaction with bromine water is like that of the other diene sulfo acids. The structure of the sulfo acid was fixed by oxidizing an aqueous solution of its sodium salt. There is no doubt that oxidation took place at the double bonds:



$$CH_2{=}\underset{CH_3}{C}{-}\underset{CH_3}{C}{=}CH{-}SO_3Na \xrightarrow{+\,O} O\underset{CH_3}{C}{-}\underset{CH_3}{C}O + SO_4''$$

The reaction products included diacetyl, which was converted into dimethylglyoxime, which exhibited the characteristic rose-colored precipitate of the coordination compound with nickel sulfate (L.A.Chugaev's reaction [26]).

As our preliminary tests have shown, other dienes – such as piperylene, hexadiene-2,4, 2,4-dimethylpentadiene-2,3 – can also be sulfonated with pyridine sulfotrioxide. We have not established the composition or structure of the resulting sulfo acids as yet.

EXPERIMENTAL

Sulfonation of divinyl. 96 g (0.6 mole) of pyridine sulfotrioxide and a solution of 25 ml (0.3 mole) of commercial drivinyl* in 25 ml of dichloroethane were heated together to 100-110° for 10 hours in a 500-ml stainless-steel autoclave. No pressure nor odor of sulfur dioxide was noticed when the autoclave was opened. The light-yellow sulfo mass, which had melted together, was treated with 100 ml of 20% ammonia. The sulfo product dissolved rapidly with the evolution of a small amount of heat. The separated layer contained, besides 25 ml of dichloroethane and 45 ml of pyridine, a certain amount of the ammonium salt of an unsaturated sulfo acid, which was left behind when the solvents were driven off. The salt was combined with the bulk of the aqueous ammonia layer. In addition, some 2 g of a spongy polymer was recovered from the sulfonation products. The water-ammonia layer was extracted several times with benzene to remove the last traces of pyridine. 200 g of barium hydroxide was added to the aqueous solution to precipitate the sulfates and drive out the ammonia. The mixture was then evaporated to dryness. The residue was extracted with water. The excess barium hydroxide was precipitated with carbon dioxide. The filtrate was evaporated to dryness. Inasmuch as it proved difficult to get rid of the residual water, the crude salt was desiccated by boiling it with benzene. This yielded 51.6 g (77%) of a crystalline anhydrous barium salt of a monosulfo acid.

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*Commercial divinyl usually contains about 10% of pseudobutylene. But experiment has shown that this monolefin practically does not react with pyridine sulfotrioxide.

6.222 mg substance : 3.609 mg $BaSO_4$. Found %: Ba 34.13.
$(C_4H_5O_3S)_2Ba$. Computed %: Ba 34.03.

The potassium and sodium salts were prepared by precipitating the barium salt with solutions of the respective sulfates. The anhydrous salts were secured by boiling with benzene to remove any residual water. The m.p. of the potassium salt was 210°. Decomposition set in above 240°.

8.720 mg substance: 8.884 mg CO_2; 2.610 mg H_2O. 3.810 mg substance: 1.920 mg K_2SO_4. Found %: C 27.72; H 3.35; K 22.62.
$C_4H_5O_3SK$. Computed %: C 27.89; H 2.93; K 22.70.

Analysis of the primary product of the sulfonation of divinyl. 10.8 g (0.2 mole) of pure divinyl, prepared by treating 1,2,3,4-tetrabromobutane with zinc dust, was heated in a sealed tube to 100-110° with 16 g of pyridine sulfotrioxide (0.1 mole) and 19 ml of dichloroethane. After all the pyridine sulfotrioxide had reacted (within 8 hours) the tube was opened. The excess divinyl and dichloroethane was driven off. The sulfo mass - the primary product - was a thick, light-yellow liquid, which was carefully treated several times with absolute ether (the sulfo product did not dissolve in the ether). The residual ether was driven off by heating over a water bath.

Analysis of the primary sulfonation product. 7.630 mg substance: 12.580 mg CO_2; 2.880 mg H_2O. 3.500 mg substance: 5.780 mg CO_2; 1.330 mg H_2O. 8.380 mg substance: 0.549 ml N_2 (741 mm, 22°). 6.710 mg substance: 0.439 ml N_2 (741 mm, 22°). Found %: C 44.96, 45.04; H 4.22, 4.25; N 7.38, 7.38. $C_4H_6(C_5H_5NSO_3)_2$. Computed %: C 45.15; H 4.33; N 7.52.

2.65 g of the primary product was dissolved in 50 ml of water and brought to a boil. A solution of barium chloride was added. The precipitated barium sulfate weighed 1.64 g. The usual treatment with ammonia and caustic baryta yielded the barium salt, which was converted into the potassium salt. Analyses of these salts indicated they were the same as the substances secured from commercial divinyl.

The α-divinylsulfo acid (butadiene-1,3-sulfonic-1 acid) was recovered in the free state from a 10% solution of the barium salt by adding to it an equivalent quantity of dilute sulfuric acid. The filtrate, containing the divinylsulfo acid, exhibited no signs of decomposition after prolonged storage (about 1½ years). The solution of the acid was placed in a porcelain dish in a vacuum desiccator above sulfuric acid for a few days. The contents of the dish gradually darkened as the water was eliminated. The residue was dark brown and deliquesced in the air. Aqueous solutions of the divinylsulfo acid exhibited a strong acid reaction. The acid did not dissolve in ordinary organic solvents, with the exception of alcohols. Concentrating the acid by evaporation over a water bath caused rapid darkening, accompanied by decomposition of the acid, the sulfo group being detached as a sulfate ion and tarry substances being formed

Reduction of a salt of the divinylsulfo acid. A solution of 7 g (0.04 mole) of the potassium salt in 50 ml of water was hydrogenated in a "duck" at room temperature with Raney nickel (about 10 g). Hydrogen was passed through until no more was absorbed. 900 ml (0.04 mole) of hydrogen was absorbed in 6 hours. The catalyst was filtered out, and the filtrate was evaporated. This yielded 7 g of a white crystalline salt. A solution of this salt decolorized permanganate and bromine water.

6.481 mg substance: 3.264 mg K_2SO_4. Found %; K 22.60.
$C_4H_7O_3SK$: Computed %: K 22.44.

Oxidation of the reduced salt. Slightly more than 4 atoms of oxygen were used per mol of the hydrogenated salt. 9.5 g (0.06 mole) of potassium permanganate was added a little at a time, with frequent shaking, to 3.5 g (0.02 mole) of the potassium salt dissolved in 25 ml of water. Manganese dioxide and carbon dioxide began to be evolved at once, accompanied by the evolution of heat. Toward the end of the reaction, the mixture was heated slightly over a water bath. The filtrate was evaporated to small volume. After acidulation with sulfuric acid the characteristic odor of propionic acid appeared. The latter was distilled with steam. The distillate was neutralized with ammonia and treated with a solution of silver nitrate. The white crystalline precipitate was freed of its excess $AgNO_3$ and dried in the dark at 60-70° after double recrystallization from hot water.

8.345 mg substance: 4.983 mg Ag. Found %: Ag 59.71. $C_3H_5O_3Ag$.
Computed %: Ag 59.62.

Action of bromine upon a salt of the divinylsulfo acid. An accurately weighed sample of the sodium salt was dissolved in 20 ml of water in a small flask with a ground-glass stopper. An accurate solution of bromine in methanol was added to the solution from a buret. Decolorization was rapid. The flask was agitated for 10-15 minutes to complete the reaction, and then the reaction mixture was neutralized with alkali. The amount of bromine ion formed was determined by titration with a 0.2 *N* solution of $AgNO_3$ in the presence of K_2CrO_4.

1) 0.5374 g substance: 0.5501 g of bromine added, 17.80 ml of 0.2 *N* $AgNO_3$ solution being used to titrate the bromine ion, i.e., the bromine ion totaled 0.2324 g, or 51.34% of the bromine used for the reaction.

2) 0.6286 g substance: 0.6434 g of bromine added, 20.54 ml of 0.2 *N* $AgNO_3$ solution being used to titrate the bromine ion, i.e., the bromine ion totaled 0.3258 g, or 50.63% of the bromine used for the reaction.

Synthesis of $(CH_2{=}CH{-}CH{=}CBrSO_3)_2Ba$. Bromine was added to a solution of the barium salt or to the free divinylsulfo acid until the solution had a faint color that did not disappear. Air was passed through the solution to remove the excess bromine. The reaction mixture was treated with a paste of barium carbonate and silver (prepared with 4 parts of barium carbonate and 1 part of silver nitrate) to remove the bromine ion. Evaporation of the filtrate over a water bath yielded a white crystalline salt, a solution of which no longer decolorized bromine water.

6.124 mg substance: 2.561 mg $BaSO_4$. 8.345 mg substance: 5.589 mg AgBr.
Found %: Ba 24.61; Br 28.50. $(C_4H_4O_3SBr)_2Ba$. Computed %: Ba 24.45;
Br 28.47.

Acid chloride of the divinylsulfo acid. 7 g of the sodium salt was triturated in a porcelain dish with three times the amount of phosphorus pentachloride. The mixture melted and heated up within a few minutes. The dish was cooled to prevent excessive heating. Continuous stirring is required for this reaction. If the onset of the reaction is slow, the mixture should be heated slightly on a water bath. The reaction mass was treated with ether three times. The ether extract was washed repeatedly with ice water to remove the oxychloride and the excess phosphorus pentachloride. This caused part of the acid chloride to polymerize. Then the extract was desiccated with calcium chloride.

Anilide of the divinylsulfo acid. To an ether solution of the acid chloride there were added an equal quantity of aniline and about 0.5-1 ml of pyridine. The mixture was heated for 2 hours with a reflux condenser. A layer of red liquid separated at the bottom of the flask. After the solvent had been decanted, the solidified mass was treated with sulfuric acid and washed thoroughly with hot and cold water. The resulting bright red crystals were petal shaped and had a m.p. of 83°.

7.255 mg substance: 0.434 ml N_2 (17°, 738 mm). Found %: N 6.34.
$C_{10}H_{11}O_2SN$. Computed %: N 6.69.

Sulfonation of isoprene. 7 g (0.1 mole) of isoprene (b.p. 33.5°; d_4^{20} 0.6300, n_D^{20} 1.4213) was sulfonated by heating it to 100° for 8 hours with 32 g of pyridine sulfotrioxide (0.2 mole) dissolved in 10 ml of dichloroethane, to which 0.5% of m-dinitrobenzene had been added. The processing of the sulfonation product was similar to that used for the divinyl. We secured 13 g (58%) of a barium salt, which was purified by reprecipitation from an aqueous solution of methanol. The salt was freely soluble in water, but only very slightly soluble in alcohol

3.655 mg substance: 1.932 mg $BaSO_4$. 4.400 mg substance: 2.350 mg $BaSO_4$.
Found %: Ba 31.91, 31.43. $(C_5H_7O_3S)_2Ba$. Computed %: Ba 31.80.

The sodium salt was prepared by precipitating a solution of the barium salt with sodium sulfate. White crystals, freely soluble in water, but only slightly soluble in alcohol.

6.210 mg substance: 2.648 mg Na_2SO_4. 8.228 mg substance: 3.500 mg Na_2SO_4. Found %: Na 13.81, 13.77. $C_5H_7O_3SNa$. Computed %: Na 13.51.

When salts of the isoprenesulfo acid are reacted with a solution of potassium permanganate, oxidation is perceptible even in the cold. After the manganese dioxide had been dissolved by hydrochloric acid, a white precipitate of barium sulfate was left. Bromine water reacts readily with the barium salt, barium sulfate not separating out even when heated.

Determination of the structure of the isoprenesulfo acid. 2.7 g (0.014 mole) of the potassium salt was dissolved in 30 ml of water and hydrogenated in a "duck" at room temperature with 5 g of Raney nickel. 320 ml (0.0143 mole) of hydrogen was absorbed in 6 hours. A solution of 2.5 g of the reduced salt was oxidized with 4.9 g of potassium permanganate. 10 ml of liquid was distilled from the liquid. In the distillate we found methyl ethyl ketone, identified by the melting point of its p-nitrophenylhydrazone (125-126° [27]). A test sample, mixed with a known sample, exhibited no depression.

Sulfonation of 2,3-dimethylbutadiene. Di-isopropenyl was prepared by dehydrating pinacol by heating it with iodine [28]. The purified hydrocarbon had a b.p. of 69.5-70.5°; d_4^{20} 0.7270; n_D^{18} 1.4360. 5 g (0.06 mole) of di-isopropenyl was heated to 100° for 8 hours with 19 g (0.12 mole) of pyridine sulfotrioxide dissolved in 7 ml of dichloroethane, to which 0.05 g (1%) of m-dinitrobenzene had been added. Treatment of the sulfo mass like that used above yielded 12 g of the barium salt (57%).

2.326 mg substance: 1.292 mg $BaSO_4$. Found %: Ba 32.69.
$(C_6H_9O_3S)_2Ba$. Computed %: Ba 29.86. $C_6H_8O_6S_2Ba$. Computed %: Ba 36.80.

A saturated solution of 8 g of the barium salt was precipitated with methanol. The precipitated salt exhibited a lower barium content. Triple reprecipitation yielded 4 g of a salt of a monosulfo acid.

4.261 mg substance: 2.439 mg $BaSO_4$. 5.324 mg substance: 3.054 mg $BaSO_4$. Found %: Ba 30.22, 30.79. $(C_6H_9O_3S)_2Ba$. Computed %: Ba 29.86.

The sodium salt of a monosulfo acid was prepared by precipitating the barium salt with sodium sulfate.

6.815 mg substance: 2.660 mg Na_2SO_4. 4.342 mg substance: 1.732 mg Na_2SO_4. Found %. Na 12.62, 12.89. $C_6H_9O_3SNa$. Computed %: Na 12.47.

Determination of the structure of the sulfo acid of dimethylbutadiene. About 6 g of finely pulverized potassium permanganate was added a little at a time to 1.5 g of the salt dissolved in 40 ml of water in a distilling flask. At the same time the oxidation product was distilled with steam. The distillate was heated with a small amount of hydroxylamine hydrochloride, the solution was neutralized with ammonia, and a few drops of a solution of nickel sulfate were added. The solution soon turned rose-colored. The next day the characteristic scarlet-red precipitate of the nickel-dimethylglyoxime coordination compound settled out.

SUMMARY

1. Divinyl and its homologs – isoprene and di-isopropenyl – have been sulfonated by heating in sealed tubes with an excess of pyridine sulfotrioxide.

2. It has been shown that diene monosulfo acids were formed in every case, with the sulfo group at the end of the conjugated system, which have never been previously described in the literature.

3. Butadiene-1,3-sulfonic-1, 2-methylbutadiene-1,3-sulfonic-1, and 2,3-dimethylbutadiene-1,3-sulfonic-1 acids have been synthesized for the first time as their barium salts.

4. The example of divinyl has been used to show that pyridine sulfotrioxide forms a primary sulfonation product with a diene in the molecular proportions of 2:1.

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A STUDY OF SULFONATION REACTIONS

XVI. EQUILIBRIUM BETWEEN A SULFO ACID AND ITS ACID CHLORIDE

A. A. Spryskov and Yu. L. Kuzmina

Either sulfo acids or acid chlorides of sulfo acids are produced by the action of chlorosulfonic acid on various organic compounds. When 1 mol or some what more of chlorosulfonic acid is used per mol of the substance to be sulfonated, the sulfonation reaction proceeds as follows:

$$RH + HSO_3Cl \longrightarrow RSO_3H + HCl. \qquad (I)$$

If a large excess of chlorosulfonic acid is used (3-4 mols), compared to the sulfonated reagent, it is mainly the acid chloride that is formed, and the reaction chiefly takes this course:

$$RH + 2HSO_3Cl \longrightarrow RSO_2Cl + H_2SO_4 + HCl. \qquad (II)$$

The yield of the acid chloride never attains the theoretical, however, and only rarely approaches it. This is due to the fact that the sulfuric acid evolved during the reaction converts the acid chloride into the sulfo acid as follows:

$$RSO_2Cl + H_2SO_4 \rightleftarrows RSO_3H + HSO_3Cl. \qquad (III)$$

The latter reaction is an equilibrium one, so that increasing the excess of chlorosulfonic acid in the mixture increases the yield of the acid chloride. Since a large excess of chlorosulfonic acid is used to prepare acid chlorides, all the sulfonated reagent is converted into a sulfo derivative, while the hydrogen chloride leaves the reaction zone as a gas, so that when sulfonation is complete, the system consists of the four constituents of the last equation. It is easy to calculate the most advantageous proportions of the reagents, provided the equilibrium constant of this reversible reaction is known. Let $\underline{n}$ mols of chlorosulfonic acid be used in sulfonation per mol of the organic substance; then we will have $\underline{x}$ mols of the sulfo acid and $1 - x$ mols of the acid chloride after the reaction is complete and equilibrium has been attained. $1 - \underline{x}$ mols of sulfuric acid have been produced [cf Equation (II)], and $2(1 - \underline{x})$ mols [cf Equation (II)] and $\underline{x}$ mols [cf Equation (I)] of chlorosulfonic acid will have been expended. The chlorosulfonic acid remaining will then be $\underline{n} - 2(1 - \underline{x}) - \underline{x}$, and the equilibrium constant will be given by the equation:

$$K = \frac{[RSO_3H]\cdot[HSO_3Cl]}{[RSO_2Cl]\cdot[H_2SO_4]} = \frac{[\underline{x}]\cdot[n - 2 + \underline{x}]}{[1 - \underline{x}]^2}. \qquad (IV)$$

During the past few years the production of the acid chlorides of sulfo acids has become very important in practice, which impelled us to undertake to prove the existence of this equilibrium system and to find some equilibrium constant for an acid chloride and its sulfo acid in a mixture of chlorosulfonic acid and sulfuric acid. We chose p-toluene sulfochloride as our research object; it was mixed with chlorosulfonic and sulfuric acids in various proportions at 0°. The mixture was kept in thawing snow for various intervals of time to make it possible to observe the attainment of a state that was close to equilibrium by gravimetrically determining the amount of the chloride still left after the mixture had been poured out over ice.

When 100% chlorosulfonic acid is used in sulfonation, the number of mols of sulfuric acid formed equals the number of mols of the chloride; in our tests we used various numbers of mols of sulfuric acid, so that the formula derived for the equilibrium constant had to be changed. If we take 1 mol of the chloride, $\underline{m}$ mols of sulfuric acid, and $\underline{n}$ mols of chlorosulfonic acid, the equilibrium constant will be given by the equation:

$$K = \frac{[\underline{x}]\,[n + \underline{x}]}{[1 - \underline{x}]\cdot[m - \underline{x}]} \qquad (V)$$

after equilibrium has been reached, in accordance with:

$$\underset{1 - \underline{x}}{RSO_2Cl} + \underset{m - \underline{x}}{H_2SO_4} \rightleftharpoons \underset{\underline{x}}{RSO_3H} + \underset{n + \underline{x}}{HSO_3Cl}. \qquad (III)$$

The results of our tests are summarized in Table 1, which shows that a state close to that of equilibrium is attained within 4 to 9 hours or more, inasmuch as the quantity of unchanged chloride remains practically constant in the individual samples of any single run, continued for various periods of time. Our observations indicate that somewhat more time is required to reach a state close

TABLE 1

The state of equilibrium between p-toluenesulfo acid and its acid chloride at 0°

Test No.	Mols used per mol of the chloride		Mixture reaction time, hours	Chloride recovered, % of initial amount	Equilibrium constant, $\underline{K}$
	H_2SO_4	HSO_3Cl			
36	1.14	4.99	6	82.3	1.16
			9	81.4	1.24
39	1.74	4.70	6	68.6	1.64
			9	69.2	1.55
33	2.53	3.58	0.5	59.7	
			2	58.8	
			4	57.8	1.39
			6	57.7	1.39
34	3.99	2.96	0.5	50.9	
			2	50.5	
			4	48.7	1.05
			6	47.6	1.10
37	4.99	2.43	8	42.9	
			22	41.5	0.97
			32	42.2	0.94
			9	35.5	
38	6.39	2.05	22	34.3	0.90
			32	34.1	0.91
				Average .... K =	1.18

to equilibrium for mixtures containing less chlorosulfonic acid, so that in Tests 37 and 38 the constants were computed from the results of analysis of samples kept for 22 to 32 hours. Our experimental results also indicate that the equilibrium constant varied somewhat more than 50% in the various tests, whereas the sulfuric – chlorosulfonic acid ratio varied by a factor of 15. The quantity of acid chloride converted into the sulfo acid also varied throughout a wide range: from 18 to 66%. Using the value of the equilibrium constant we have found, the amount of the sulfo acid may be calculated from:

$$\underline{x} = \frac{n + K + Km \pm \sqrt{(n + K + Km)^2 - 4(K - 1)Km}}{2(K - 1)} \qquad \text{(VI)}$$

Table 2 gives the amount of the acid chloride $(1 - x)$, as computed from this equation, together with the mean observed experimental values after a state approaching equilibrium had been reached (within 4-9 or 22-32 hours).

TABLE 2

Equilibrium between p-toluenesulfo acid and its acid chloride

Test No.	Sulfochloride in the mixture, % of the initial amount		Discrepancy, %
	Observed	Computed	
36	81.9	81.9	0
39	68.9	73.9	-5.0
33	57.8	60.6	-2.8
34	48.2	46.1	+2.1
37	41.9	37.5	+4.4
38	34.2	29.2	+5.0

TABLE 3

Equilibrium of the reaction between acetic acid and alcohol

Mols of alcohol used	Mols of ester		Discrepancy, %
	Observed	Computed	
0.5	0.429	0.423	+0.6
0.67	0.546	0.525	+2.1
1.0	0.665	0.667	-0.2
1.5	0.779	0.785	-0.6
2.0	0.828	0.845	-1.7
3.0	0.882	0.903	-2.1
4.0	0.902	0.930	-2.8
5.4	0.920	0.949	-2.9

By way of evaluating these results, let us cite the classic example of equilibrium in liquid systems – the reaction between alcohol and acetic acid [1]. As we know, the equilibrium constant of this reaction is 4. We see in Table 3 that the discrepancy between the computed and the observed values is as much as 2.9% in the esterification reaction, this discrepancy going as high as 5% in our experiments on the equilibrium of p-toluenesulfo acid and its acid chloride.

Aside from experimental errors, there are two reasons for the discrepancy between the computed and the observed values. The first source of error is the partial hydrolysis of the chloride, which takes place when the reaction mixture is poured over the ice; this has been demonstrated in our tests, described in the experimental section below. The second source of error is the partial sulfonation of the chloride (or of the sulfo acid) while the mixture is set aside to stand, since it has been noticed that the chloride recovered from the mixture has a lowered melting point (about 60°), owing to the formation of a disulfochloride. The presence of the latter was demonstrated by analyzing the chloride; after hydrolysis it required 4.5% more 0.1 $\underline{N}$ alkali than it should have according to calculation, i.e., the chloride recovered contained about 4% of a disulfo derivative.

EXPERIMENTAL

100% sulfuric acid was prepared from oleum by driving off the sulfuric anhydride and absorbing the chemically pure sulfuric acid. Analysis of the resultant reagent showed that it contained an average of 100.17% of H_2SO_4. The chlorosulfonic acid was distilled at 86-89° and a vacuum of 22-35 mm; it was analyzed by titrating a weighed sample in an ampoule with 0.1 N alkali solution. Since the equivalent of the sulfuric acid was 49.05, and that of the chlorosulfonic acid was 38.84, the percentage of sulfuric acid in the chlorosulfonic acid can be calculated to determine the equivalent. Titration of two weighed samples of the resulting transparent and colorless chlorosulfonic acid gave its equivalent as 38.94 and 38.91. The p-toluenesulfo acid was purified by recrystallizing it from ether; its m.p. was 69.5°. Before investigating the equilibrium we ran tests to determine the amount of the chloride that was hydrolyzed when the mixture was poured over ice and when it was washed on the filter. This was done by dissolving a weighed sample of the chloride in the chlorosulfonic acid, pouring the solution over ice, filtering out the chloride, washing it, drying it in a desiccator, and weighing it. The test results listed in Table 4 indicate that the losses due to hydrolysis total some 2%, and those due to washing some 0.4%. The losses of the chloride during washing, without dissolution in the chlorosulfonic acid, were determined from Tests 25 and 28. Our measurements indicate that the losses of chloride during drying in the desiccator or above pieces of caustic soda do not exceed 0.1% of the initial total.

TABLE 4

Losses of chloride due to hydrolysis and washing it with ice water

Test No.	Amount taken		Amount of water used in washing, ml	Losses of chloride, % initial amount
	Chloride, grams	HSO_3Cl, grams		
21	1.061	1.76	120	2.4
26	0.887	1.76	120	2.9
29	0.937	1.76	120	2.0
25	1.068	–	120	0.4
28	0.753	–	120	0.4

The acid chloride recovered from the reaction mixture had a melting point of about 60°, since it underwent partial sulfonation by the chlorosulfonic acid, forming a disulfochloride. The presence of the disulfochloride was detected by using 0.1 N alkali to titrate a weighed sample of the hydrolyzed chloride, which forms two equivalents of the acid upon hydrolysis, whereas the disulfochloride forms four equivalents of the acid. Samples weighing about 0.2 g of the chloride were first hydrolyzed in a sealed tube with 4 ml of water and 1 ml of alcohol. The solid phase usually disappeared after heating had gone on for 4-5 hours, but heating was continued for 8 to 48 hours at 102° and for 30 hours at 120°. The test results, listed in Table 5, show that hydrolysis of the chloride in an acid medium does not go to completion even when heating is continued for an extraordinarily long time. When the chloride was heated with a 0.1 N solution of alkali (slightly in excess of the calculated quantity), hydrolysis was completed within 5 hours after heating ceased. After the heating with alkali, the excess of the latter was titrated back with a 0.1 N solution of hydrochloric acid, a correction (about 0.1 ml) being added for the dissolving of the glass, as determined in a special test by heating 0.1 N alkali in the same glass container. Comparison of the results listed in the last two columns of Table 5 shows that the product recovered from the equilibrium mixture contains about 4% of a disulfochloride, which was one of the sources of error in our equilibrium investigation.

SUMMARY

It has been found that when p-toluenesulfo acid is heated in a mixture of chlorosulfonic and sulfuric acids, it is converted into a sulfo acid until the

TABLE 5

Hydrolysis and Titration of p-Toluene Sulfochloride

Test No.	Hydrolyzing medium	Temperature	Heating time, hours	Amount of 0.1 N alkali used (% of the calculated amount)	
				Pure chloride	Recovered chloride
56	Alcohol and water ..	102°	8	94.6	100.7
59	Ditto	102	25	96.7	100.8
61	Ditto	102	48	97.6	101.5
66	Ditto	120	30	98.2	103.5
71	0.1 N alkali	100	5	99.5	104.5
72	Ditto	100	10	99.2	-

chloride and the sulfo acid reach equilibrium, which depends upon the amounts of the chlorosulfonic and sulfuric acids present. The equilibrium constant has been found to be 1.18 at 0°. The composition of the equilibrium mixture may be computed within ± 5%. A state approaching that of equilibrium is reached within 4 to 9 hours or a little longer.

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THE ACTION OF INHIBITORS IN THE CATALYTIC HYDROGENATION OF SOME ACETYLENIC AND ETHYLENIC ALCOHOLS. II

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It is common knowledge that acetylenic-γ-glycols quickly add only 2 atoms of hydrogen per molecule of the glycol in the presence of colloidal palladium [1], whereas acetylenic alcohols add 4 atoms of hydrogen and are readily converted into saturated alcohols [2].

The problem of whether acetylenic alcohols can be hydrogenated with colloidal palladium under conditions that make it possible to inhibit the process abruptly after the first two hydrogen atoms have been added, thus giving rise to an ethylenic alcohol, is an interesting one, however.

In this connection it was useful to determine what influence the inhibitors would have on the hydrogenation of acetylenic alcohols – whether they would set up the necessary favorable conditions.

Our previous researches, in association with Yu.S.Zalkind [3], covered tetramethylbutyldiol, dimethylacetylenylcarbinol, and dimethylvinylcarbinol. We found that when these compounds were hydrogenated in the presence of colloidal palladium, certain substances, such as copper acetate, lead acetate, ammonium thiocyanate, and thiourea, slow down the hydrogenation in varying degree. Potassium cyanide, sodium arsenide, sodium arsenate, and nickel and cobalt sulfates do not affect the reaction rate under similar conditions. We noticed that the hydrogenation of an acetylenic alcohol was less sensitive to the action of an inhibitor than the hydrogenation of a glycol; the hydrogenation of an ethylenic alcohol was somewhat more sensitive than that of an acetylenic alcohol, but less so than that of a glycol. Moreover, an ethylenic alcohol used in ready form was hydrogenated more slowly than the same acid formed during the addition reaction of two atoms of hydrogen to an acetylenic alcohol. There was, therefore, no doubt about the somewhat selective nature of the action of these inhibitors.

On the other hand, we surmised, from our observations, that an inhibitor acted upon the substance to be hydrogenated, rather than upon the catalyst. We assumed that the inhibitor (I) formed an adsorption or chemical compound with the reacting substance (S), the resulting compound being able to dissociate as follows: $I + S \rightleftarrows IS$. We conjectured that these IS compounds arise from the active form of the acetylenic or ethylenic alcohol and the unshared electron pairs of the elements constituting the inhibitor.

We decided to continue our research, with the objective of ascertaining the influence of other substances as inhibitors as well as the manner of their action. Starting with the foregoing conjecture that substances possessing atoms with unshared electron pairs ought to act as inhibitors of the hydrogenation of acetylenic and ethylenic alcohols in the presence of colloidal palladium, we chose for our first tests thiocyanogen derivatives: benzene thiocyanate, p-thiocyanoaniline, p-thiocyanochlorobenzene, and α-naphtholthiocyanate, plus chlorobenzene for the sake of comparison. At the same time we investigated the effect of benzene, aniline, naphthalene, α-naphthol, β-naphthol, and the methyl ester of the latter to determine the part played by the aromatic radical attached to the thiocyanogen group. The following acetylenic alcohols were hydrogenated: 2-methyl-3-butynol-2 and 3-methyl-1-pentynol-3; the ethylenic alcohols hydrogenated were: 2-methyl-3-butenol-2; 3-methyl-1-pentenol-3. For the sake of brevity, we shall call these alcohols henceforth methylbutynol, methylpentynol, methylbutenol, and methylpentenol, respectively. The catalyst was prepared by dissolving palladium in aqua regia and then evaporating the solvent; gum arabic served as the protective colloid [4]. Colloidal palladium was prepared in a single batch for a series of tests, its action being tested by hydrogenating tetramethylbutynediol (the acetylenic γ-glycol on which the most research has been done in this regard) and a corresponding alcohol without the use of an inhibitor.

The concentration of the palladium solution was determined by evaporating a sample, calcining the residue, and weighing the metallic palladium. The solution was adjusted to contain 1 mg of palladium per ml of solution. The resulting colloidal solutions were stable.

TABLE 1

Methylbutynol dissolved in distilled water: 0.84 g methylbutynol (0.01 mol); 3 mg Pd; and 50 ml of water

Addition time without inhibitor: 13 minutes for 2 H; 30 minutes for 4 H

Inhibitor	Amount of inhibitor (% of methylbutynol)	Addition time, min.		Conclusion	
		2H	4H	Inhibition	
				During first half	During second half
Phenyl mustard oil..........	0.007	16	30	Almost imperceptible	Imperceptible
α-Naphtholthiocyanate.......	0.048	16	36	Very slight	Very slight
	0.095	44	75% in 90 minutes	3.4 times	Greatly inhibited

The experiments were run in a specially equipped thermostat cabinet at 20°. The hydrogen was produced by electrolyzing a 10% solution of sodium hydroxide. Hydrogenation was effected in a long-necked flask with a side branch tube that reached to the middle of the flask. The flask was rocked at a constant rate – 120 per minute. In each experiment we used 0.01 mol of the alcohol under test, 50 ml of solvent, and 3 or 5 mg of palladium. The tests and comparisons were run separately for hydrogenation with 3 mg and 5 mg of palladium. The alcohols to be hydrogenated were purified by repeated distillation. Methylbutynol had a b.p. of 103-105°; methylbutenon a b.p. of 98-99°; methylpentynol a b.p. of 119-120°, and methylpentenol a b.p. of 114-115°. All the inhibitors and additives used were chemically pure.*

We performed a few tests in aqueous solution. Most of the hydrogenation runs were made in a solution of ethyl alcohol. The results of our investigations are given in several tables.

Table 1 indicates that α-naphthol thiocyanate is a powerful inhibitor when taken in 0.095% by weight of the acetylenic alcohol, inhibiting the addition of hydrogen to methylbutynol very markedly during the second half of the hydrogenation period, i.e., during the transformation of the double bond into a single one. Phenyl mustard oil, in very low concentration (0.007% of the alcohol), has practically no effect upon the rate of hydrogenation of methylbutynol in aqueous solution.

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*Some substances wete kindly made available to us by A. I. Kulikov.

This same acetylenic alcohol (methylbutynol) was then hydrogenated in an ethyl alcohol solution with 5 and with 3 mg of palladium (Tables 2 and 3).

TABLE 2

Methylbutynol dissolved in ethyl alcohol: 0.84 g of methylbutynol (0.01 mol); 5 mg of Pd; and 50 ml of ethyl alcohol

Addition time without inhibitor: 5 min. for 2 H; 10 min for 4 H.

Inhibitor	Amount of inhibitor (% of methylbutynol)	Addition time, minutes		Conclusion	
				Inhibition	
		2H	4H	During first half	During second half
Benzene	0.357	7-8	15	1.5 times	1.5 times
Aniline	23.8	6	18	Almost imperceptible	1.8 times
Chlorobenzene	0.048	12	47	2.4 times	4.7 times
Benzene thiocyanate.....	0.024	Up to 49% in 60 min.	Up to 24.5% in 60 min.	Quite great	Quite great
p-Thiocyandchlorobenzene	0.238	38.4% in 80 min.	19.2% in 80 min.	Very great	Very great
p-Thiocyanochlorobenzene	0.048	33	Up to 71.3% in 70 min.	6.6 times	Very great
p-Thiocyanoaniline......	0.024	14	30	2.8 times	3 times

Inspection of the data in Table 2 indicates that chlorobenzene, benzene, thiocyanate, p-thiocyanochlorobenzene, and p-thiocyanoaniline are quite active inhibitors of the hydrogenation of methylbutynol when used in amounts of 0.2 mg or 0.4 mg per 0.01 mol of the methylbutynol (0.024% or 0.048% by weight of the acetylenic alcohol). When 5 mg of palladium is used, this alcohol, without an inhibitor, adds 2 atoms of hydrogen per molecule of the alcohol in 5 minutes, adding 4 atoms in 10 minutes. With the same quantity of catalyst as before, but with 0.2 mg of benzene thiocyanate (0.024% of the alcohol) present, only 24.5% of the quantity of hydrogen required for conversion to a saturated alcohol was added in 60 minutes. Though chlorobenzene and p-thiocyanochlorobenzene slow down the reaction rate more effectively during the second half of the hydrogenation period than during the first, their action is not as pronounced during the hydrogenation of an acetylenic γ-glycol, as we saw. In other words, though we see a clearly selective action of some of the substituents, this selectivity is still not marked enough. These tests likewise show that p-thiocyanochlorobenzene is a stronger inhibitor than benzene thiocyanate, and that the latter is stronger than chlorobenzene.

Aniline, even when used in very large quantities, such as 200.0 mg per 0.84 g of methylbutynol (23.8% of the alcohol, 4,000.0% of the palladium) did not retard hydrogenation during the first half, while its inhibiting action was slight during the second half. Nor can benzene be considered an inhibitor; though it does effect some delay in hydrogenation, this delay is produced only when it is used in rather large quantities: 3 mg of benzene per 0.01 mol of the alcohol slows hydrogenation down by a factor of, say, $1\frac{1}{2}$, whereas the substances that we regard as inhibitors produce an appreciable retardation of the hydrogenation rate when added in quantities that are 10 to 20 times less than that. Henceforth we shall not regard substances that act like aniline or benzene as inhibitors.

TABLE 3

Methylbutynol dissolved in ethyl alcohol: 0.84 g methylbutynol (0.01 (0.01 mol); 3 mg Pd; and 50 ml ethyl alcohol

Addition time without inhibitor: 7 minutes for 2 H; 12-15 minutes for 4H.

Inhibitor	Amount of inhibitor (% of methylbutynol)	Addition time, minutes		Conclusion — Inhibition	
		2H	4H	During first half	During second half
Naphthol thiocyanate..............	0.048	7	85	Imperceptible	6-7 times
Naphthalene........	0.048	5	10-12	Some acceleration	Some acceleration
α-Naphthol.........	0.048	5	10	Ditto	Ditto
β-Naphthol.........	0.095	5	12	Ditto	Ditto
Methyl ester of β-naphthol	0.095	4	9	50% acceleration	50% acceleration
Phenyl mustard oil.	0.007	7	17	Almost imperceptible	Hardly noticeable
Phenyl mustard oil..	0.014	8	23	Hardly noticeable	1.5-2 times
Phenyl mustard oil.	0.024	18	35	3 times	2.5-3 times

The data in Table 3 show that α-naphthol thiocyanate and phenyl mustard oil are active inhibitors of the hydrogenation of methylbutynol with colloidal Pd, the former displaying more selectivity that the latter in reducing the rate of hydrogenation of the triple and double bonds. When 0.4 mg of α-naphthol thiocyanate is added to 0.01 mol of methylbutynol (0.048% of the alcohol) in the presence of 3 mg of colloidal palladium, it has hardly any effect upon the rate at which hydrogen is added at the triple bond, though it reduces the rate at which the ethylenic bond is converted into a single bond by a factor of 6-7.* This is even more clearly seen in Fig. 1, in which the amount of hydrogen absorbed by the acetylenic alcohol is laid off on the axis of ordinates in per cent of 4 atoms of hydrogen per molecule of the alcohol, with the time in minutes laid off on the axis of abscissas.

The abruptness of the bend in the curve occurring after 2 atoms of hydrogen had been added per molecule of the alcohol is less, however, than when an acetylenic γ-glycol was hydrogenated with Pd [1].

The experimental results listed in Table 3 likewise indicate that naphthalene, α- and β-naphthol, and the methyl ester of the latter are not inhibitors; on the contrary, they accelerate hydrogenation somewhat, this being especially true of the ester of β-naphthol.

The next series of tests was run with methylpentynol. The results are

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*After 55% hydrogen had been added no reaction is obtained with a silver reagent for a triple bond. Bromine water is decolorized.

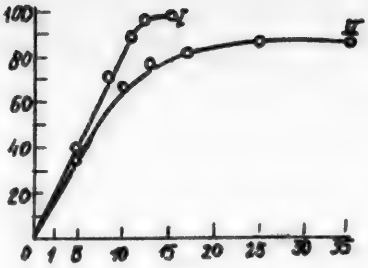

Fig. 1.

I-Methylbutynol and 3 mg of Pd in alcoholic solution; II-the same, plus 0.4 mg of γ-naphthol thiocyanate.

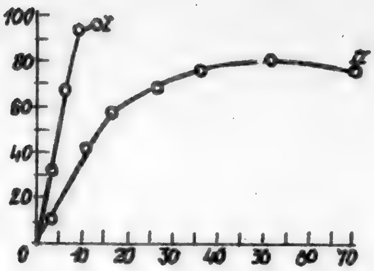

Fig. 2.

I Methylpentynol and 5 mg of Pd in an alcoholic solution; II.-the same, plus 0.4 mg of thiocyanoaniline.

listed in Table 4. They show that benzene thiocyanate, p-thiocyanochlorobenzene, phenyl mustard oil, thiocyanoaniline, and α-naphtholthiocyanate are all inhibitors of this reaction, causing about the same retardation as in the hydrogenation of methylbutynol. Only benzene thiocyanate and p-thiocyanochlorobenzene exhibited greater inhibitory action than in the reaction with methylbutynol.

TABLE 4

0.09 g methylpentynol (0.01 mol); 50 ml alcohol; 5 mg Pd
Addition time without inhibitor: 4-5 minutes for 2H; 9-11 minutes for 4H.

Inhibitor	Amount of inhibitor (% of methylpentynol)	Addition time, minutes		Conclusion	
				Inhibition	
		2H	4H	During first half	During second half
Benzene thiocyanate	0.20 0.041	12 25	55 Up to 69.2% in 55 min.	2.5-3 times 5-6 times	5-6 times Great
p-Thiocyanochlorobenzene..........	0.20 0.041	13 17	40 65	2.5-3 times 3.5-4 times	4 times 6-7 times
Phenyl mustard oil.	0.020	7	Up to 88.6% in 22 min.	Slight	2.5-3 times
Thiocyanoaniline...	0.041	13	90	2.5-3 times	8-10 times
α-Naphtholthiocyanate............	0.020 0.041	9 23	30 48	1.5-2 times 4-5 times	2.5-3 times 4.5-5 times

We should also like to call the reader's attention to one interesting conclusion that follows from a comparison of the data in Tables 3 and 4: in the hydrogenation of methylbutynol it was α-naphthol thiocyanate that exhibited an outstanding selective effect, while it was p-thiocyanoaniline that produced this effect in the reaction with methylpentynol. The selective nature of its action is clearly shown in Fig. 2.*

We secured the corresponding methylbutenol and methylpentenol by breaking off the hydrogenation of methylbutynol in the presence of α-naphthol thiocyanate and that of methylpentynol in the presence of p-thiocyanoaniline after 55% of the hydrogen required for 4 atoms of hydrogen per molecule of the alcohol had been added, the yields being 80-85% of the theoretical.

Tables 5, 6, 7, 8, and 9 list the data on the effects of the substances investigated above on the hydrogenation of the ethylenic alcohols — methylbutenol and methylpentenol — in aqueous solution and in ethyl-alcohol solution, with 3 and 5 mg of palladium. Our experiments have shown that the substances (aniline, benzene, naphthalene, α- and β-naphthol, and the methyl ester of the latter) that proved to be inert with the acetylenic alcohols do not act as inhibitors here either (for the sake of brevity we have not listed data on these substances in the tables), whereas the inhibitors tested above for methylbutenol and methylpentenol (chlorobenzene, p-thiocyanochlorobenzene, p-thiocyanoaniline, phenyl mustard oil, and α-naphthol thiocyanate) proved to be active with the ethylenic alcohols.

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*A test for a triple bond with a silver reagent was negative after 5% of the hydrogen had been absorbed. Bromine water was decolorized.

TABLE 5

0.86 g methylbutenol; 50 ml distilled water; 3 mg Pd

Addition time without inhibitor for 2H: 20 minutes

Inhibitor	Amount of inhibitor (% methylbutenol)	Addition time for 2H, minutes	Conclusion
α-Naphthol-thiocyanate	0.023	Up to 74.5% in 30 min.	Rather appreciable retardation
	0.046	Up to 70.3% in 120 min.	Considerable retardation

TABLE 6

0.86 g Methylbutenol (0.01 mol); 50 ml alcohol; 5 mg Pd

Addition time for 2H without inhibitor: 8 minutes

Inhibitor	Amount of inhibitor (% of methylbutenol)	Addition time for 2H, in minutes	Conclusion
Thiocyanoaniline............	0.023	120-150; Up to 88.8% in 120 min.	Very considerable inhibition
Thiocyanochlorobenzene.......	0.023	20-25; Up to 88.0% in 20 min.	Retarded 2.5-3 times
Chlorobenzene................	0.023	12	Retarded 1.5 times
Chlorobenzene................	0.046	15	Retarded 2 times

TABLE 7

0.86 g Methylbutenol; 50 ml alcohol; 3 mg Pd

Addition time for 2H without inhibitor: 10-12 minutes

Inhibitor	Amount of inhibitor (% of methylbutenol)	Addition time for 2H, in minutes	Conclusion
α-Naphthol thiocyanate....	0.046	Up to 13.0% in 15 minutes	Considerable inhibition
Phenyl mustard oil	0.046	0.0% in 40 min.	Complete poisoning
	0.012	115-125	Retarded 10-12 times
	0.0046	50-60; 88% in 60 min.	Retarded 5-6 times

Aniline displayed practically no inhibiting effect. When the same alcohol was hydrogenated with 5 mg of Pd, 2H were added in 15 minutes; this took 20-25 minutes with 300.0 mg of aniline (34.9% of the alcohol being hydrogenated, or

TABLE 8

1.0 g methylpentenol (0.01 mol): 50 ml alcohol; 5 mg Pd

Addition time for 2H without inhibitor: 6 minutes

Inhibitor	Amount of inhibitor (% of methylpentenol)	Addition time for 2H, in minutes	Conclusion
Benzene-thiocyanate...	0.02	16.6% in 70 min.	Very considerable inhibition
	0.02	24.9% in 85 min.	
p-Thiocyano-aniline.......	0.04	3.3% in 27 min.	Very considerable inhibition
	0.02	70	Retarded 12 times
p-Thiocyano-chlorobenzene.	0.02	10	Retarded 1.7 times
	0.04	97	Retarded 16 times
	0.04	16.0% in 8 min.	

TABLE 9

1.0 g Methylpentenol (0.01 mol); 50 ml alcohol; 3 mg Pd

Addition time for 2H without inhibitor: 10 minutes

Inhibitor	Amount of inhibitor (% of methylpentenol)	Addition time for 2H, in minutes	Conclusion
Phenyl mustard oil...........	0.02	7.6% in 35 min.	Very considerable inhibition
	0.01	23	Retarded 2.3 times
α-Naphthol thiocyanate.......	0.04	30.2% in 75 min.	Very considerable inhibition

6000% of the Pd).

As we see from our tests of other inhibitors, we never had to resort to such high percentages. Inhibitory action was usually manifested with hundredths of a percent, or at times with tenths of a percent of the inhibitor by weight of the substance being hydrogenated. With aniline, however, no inhibition was observed even when integral percentages were employed, the hydrogenation rate being slowed down somewhat only under the conditions specified (about 35% of the alcohol). This explains why we do not regard aniline as an inhibitor, compared to the other substances tested.

By way of an example of the inhibitory action of p-thiocyanoaniline, we reproduce in Fig. 3 curves for the hydrogenation of methylbutenol and methylpentenol with and without the inhibitor. The hydrogen added is plotted along the azis of ordinates as per cent of 2 atoms of hydrogen per molecule of the alcohol; the abscissas are the time in minutes.

Comparison of the data in Tables 4, 8, and 9, in Tables 2 and 6, and in Table 3 and 7 indicates that, as we stated in our first paper [3], inhibitors are more effective in the hydrogenation of ethylenic alcohols than in that of acetylenic alcohols. On the other hand, as we also pointed out at the time, a ready ethylenic alcohol is hydrogenated more slowly than the same alcohol at the instant of its formation: adding the first two hydrogen atoms to methylbutynol was completed within 5 minutes when 5 mg of Pd was present, the next two atoms of hydrogen being added to the resultant ethylenic alcohol in 5 minutes as well. Under similar conditions, the ready ethylenic alcohol (methylbutenol) was hydrogenated to a saturated alcohol in 8 minutes. This singularity, apparently, interferes with the pronounced manifestation of the above-mentioned selective effect of the inhibitor on acetylenic and ethylenic alcohols (the bend in the curve after two atoms of hydrogen have been added per mol of the alcohol is not always sharp).

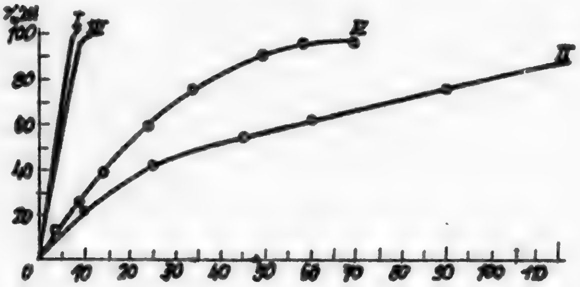

Fig. 3.

I-Methylbutenol in alcoholic solution with 5 mg of Pd; II-the same, plus 0.2 mg of p thiocyanoaniline; III-methylpentenol in alcoholic solution with 5 mg of Pd; IV-the same, plus 0.2 mg of p-thiocyanoaniline.

The mechanism of inhibitor action requires particular attention and study, owing to the complexity of the processes involved in hydrogenation. In our first paper [3] we pointed out that opinions differ as to the nature of this mechanism. Some research workers assume that the inhibitor acts upon the catalyst in some way or other, reducing its activity. Others consider that double compounds with the reagent may be formed. At the time we expressed the conjecture, in conformity with certain authors (Taylor, for instance [5]), that it is hard to give a universal explanation and that each individual case requires study if it is to be assigned to one series or another. Our past tests led us to conclude that the action of inhibitors in the hydrogenation of acetylenic and ethylenic alcohols is due to the interaction of the inhibitor with the substance being hydrogenated, rather than with the catalyst. We returned to this problem in the present investigation. Our deductions from a series of tests again led us to the same conclusion: in the hydrogenation of acetylenic and ethylenic alcohols an inhibitor renders the substance being hydrogenated inert. In fact, when a new batch of the alcohol is added after the hydrogenation reaction of an acetylenic or ethylenic alcohol has been inhibited, hydrogenation is accelerated, the hydrogen being fully added to the original alcohol as well as to the newly added batch.

For example, 0.095% of α-naphthol thiocyanate greatly inhibits the addition of hydrogen to methylbutynol, only 8-10 ml of hydrogen being absorbed per 5 minutes during the first 64 minutes after the reaction set in, but as soon as 0.001 mol of the same acetylenic alcohol had been added to the reaction flask, the hydrogenation rate rose, 47 ml of hydrogen being added during the same 5 minutes, or 96.4% of the total hydrogen required to convert the added batch of alcohol into a saturated alcohol. Another example: 0.023% of benzene thiocyanate affected the hydrogenation process so profoundly that no hydrogen at all was added during 15 minutes. Adding a new batch of the catalyst (100% of the initial quantity) produced practically no acceleration, only 9 ml of hydrogen (3.6% of 4H) being added during 30 minutes. Another experiment was even more striking: 0.023% of phenyl mustard oil caused very considerable inhibition of the addition of hydrogen to methylbutenol, only 6 ml (2.6% of 2H) being added during 35 minutes. All we had to do, however, was to add 0.5 ml of the acetylenic alcohol to the hydrogenation flask for the reaction to be accelerated considerably: 250 ml of hydrogen, i.e., 101.4% of the quantity required to convert the triple bond into a single bond, was added within 35 minutes. But the reaction did not stop there. Hydrogen continued to be added to the ethylenic alcohol at a rather high rate: another 120 ml of hydrogen was added during the next 35 minutes, after which hydrogenation continued at the rate of 10 ml of hydrogen per 5 minutes. The following experiments were especially convincing in this respect. The hydrogenation of 0.01 mole of methylpentenol was greatly retarded by the presence of 0.02% of benzene thiocyanate by weight of the substance to be hydrogenated: only 61 ml of hydrogen (24.9% of the quantity computed to be required for a single bond) being added within 85 minutes. The reaction sped up considerably after only 0.0088 mole of the acetylenic alcohol (methylpentynol) was added: 415 ml of hydrogen (96.3% of the calculated 4H for the added batch of the acetylenic alcohol) was added within 20 minutes, another 134 ml of hydrogen being added during the next 35 minutes to the initial batch of the ethylenic alcohol (95% of the quantity required for conversion into a saturated alcohol).

Phenyl mustard oil totaling 0.02% by weight of the alcohol to be hydrogenated greatly inhibited the addition of hydrogen to methylpentenol: only 19 ml of hydrogen was absorbed during 35 minutes. All we had to do, however, was to add 0.005 mole of methylpentynol to the hydrogenation flask for the reaction to speed up considerably: 218 ml of hydrogen was added in 30 minutes, and 289 ml in 45 minutes, i.e., 99% of the four atoms of hydrogen theoretically required for converting the added acetylenic alcohol into a saturated alcohol. The absorption of hydrogen continued at a rate of some 30 ml per 10 minutes. Still another example: 0.01 mole of methylpentenol was hydrogenated in the presence of 0.4 mg of p-thiocyanochlorobenzene (0.04% by weight of the alcohol). Hydrogenation was extremely slow: only 40 ml of hydrogen was absorbed in 8 minutes. After 0.009 mole of the actylenic alcohol (methylpentynol) had been added to the reaction flask, the hydrogenation rate increased abruptly: 430 ml of hydrogen, i.e., 97.8% of the quantity theoretically required for converting the acetylenic alcohol into a saturated alcohol, was added within 10 minutes. Nor did the absorption of hydrogen cease therewith: another 210 ml of hydrogen, i.e., practically as much as was needed to convert the initial batch of the ethylenic alcohol into a saturated alcohol, was added during the ensuing 25 minutes.

All this indicates that the palladium remains active, the inhibitor affecting the substance being hydrogenated. Not finding any other explanation for the present, we shall retain the hypotheses set forth above, that the inhibitor (I) forms an adsorption or chemical compound with the substance to be hydrogenated (S) and that this compound may be dissociated: $I + S \rightleftarrows IS$. The rates of the direct and reverse reactions determine the inhibitory action of the substances added during hydrogenation.

SUMMARY

An investigation has been made of the effect of inhibitors – chlorobenzene, benzene thiocyanate, p-thiocyanochlorobenzene, p-thiocyanoaniline, phenyl mustard oil, and α-naphthol thiocyanate – upon the hydrogenation of acetylenic and ethylenic alcohols in the presence of colloidal palladium, using various concentrations of these inhibitors. Under identical conditions, benzene, aniline, naphthalene, α-naphthol, β-naphthol, and the methyl ester of the latter either do not affect the hydrogenation process at all or even accelerate it somewhat, as is the case with the methyl ester of β-naphthol. The effect of the inhibitors upon the hydrogenation of acetylenic and ethylenic alcohols differs with the conditions employed. Hydrogenation of the latter alcohols is more affected by the use of inhibitors than that of the former. Moreover, ethylene alcohols, used in the ready state, are hydrogenated more slowly than the same alcohols formed during the addition of hydrogen to acetylenic alcohols.

The inhibitors α-naphthol thiocyanate (for methylbutynol) and p-thiocyanoaniline (for methylpentynol) exhibited the most selective action in the hydrogenation of acetylenic alcohols. These inhibitors may be employed for the incomplete hydrogenation of these alcohols to methylbutenol and methylpentenol, respectively.

The inhibitors act, it seems, upon the substance to be hydrogenated rather than upon the catalyst.

The results secured give reason to expect that in our future research we shall be able to hit upon even more selective inhibitors, which will enable us to hydrogenate acetylenic alcohols smoothly to ethylenic alcohols, with an even sharper bend in the hydrogenation curve, like that in the hydrogenation of acetylenic γ-glycols with colloidal palladium.

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THE ACTION OF INHIBITORS IN CATALYTIC HYDROGENATION WITH PALLADIUM III.

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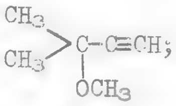
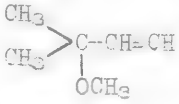
In our previous reports [1] we cited the results of our research on the effect of certain inhibitors upon the hydrogenation of acetylenic and ethylenic alcohols with colloidal palladium.

Of several tested compounds, we found that such compounds as ammonium thiocyanate, thiourea, copper and lead acetates, benzene thiocyanate, p-thiocyanoaniline, p-thiocyanochlorobenzene, α-naphthol thiocyanate, phenyl mustard oil, and chlorobenzene are inhibitors of the hydrogenation of methylbutynol, methylpentynol, methylbutenol, and methylpentenol. Some of these inhibitors manifested special selectivity in the hydrogenation of the triple and the double bond. We were interested in determining the effect of some of these inhibitors upon the hydrogenation of ethers of these alcohols. We chose as our first research objects the methyl ethers of methylbutynol (I) and of methylbutenol (II). We have found no references in the literature to methods of preparing these ethers nor to their properties, including their behavior during hydrogenation.



$(CH_3)_2C(OCH_3){-}C{\equiv}CH;$

(I)



$(CH_3)_2C(OCH_3){-}CH{=}CH$

(II)

We prepared these ethers by reacting the respective alcoholates with methyl iodide in absolute ether.

The methyl ether of methylbutynol is a mobile, colorless liquid with a pleasant odor; it forms a white precipitate with ammoniacal silver nitrate, has a b.p. of 79-80°, is soluble in many organic solvents, and is insoluble in water.

The methyl ether of methylbutenol is also a mobile, colorless liquid with a pleasant odor; it is insoluble in water and readily soluble in ether, benzene, alcohol, and other organic solvents. B.p. 82-83°. Both ethers distil under ordinary conditions without decomposing.

Both of the ethers were hydrogenated with colloidal palladium, prepared as in our previous investigations [1]; gum arabic served as the protecting colloid The catalyst's activity was checked by hydrogenating tetramethylbutynediol, methylbutynol, and methylbutenol dissolved in ethyl alcohol. Hydrogenation was carried out in a flask placed inside a thermostat cabinet (cf the description in our previous papers [1]) at 20°. 0.01 mole of substance, 50 ml of ethyl alcohol, and 3 mg (3 ml) of colloidal palladium were used for hydrogenation.

The tetramethylbutynediol was hydrogenated to a double bond in 6 minutes under these conditions, methylbutynol to a single bond in 7-8 minutes, and methylbutenol to a saturated alcohol in 3-4 minutes.

Hydrogenation of the ethers of these alcohols was very slow under the same conditions: the methyl ether of methylbutynol was hydrogenated 57.6%, based on 4 atoms of hydrogen per mol of the ether, after 320 minutes, while the ether of methylbutenol was hydrogenated 84%, based on 2 atoms of hydrogen per mol of the ether, in 260 minutes (Table 1).

This retardation is clearly seen in the diagrams (Figs. 1 and 2), in which the percent of hydrogen absorbed is laid off on the axis of ordinates, with the time in minutes along the axis of abscissas.

It is worthy of note that a test with a silver reagent for the triple bond, made after 53% of hydrogen, based on 4 atoms of hydrogen per mol of the acetylenic alcohol, had been added, was negative. This indicates that when the methyl ether of methylbutynol is hydrogenated, the hydrogen is first added at the triple bond, and then only at the double bond, i.e., as in the hydrogenation of the acetylenic alcohol itself with palladium deposited upon calcium carbonate [2]. Thus, the substitution of a methyl group for the hydroxyl hydrogen in alcohols causes a sharp decrease in the hydrogenation rate of these products. This observation fully agrees with the researches of Yu.S.Zalkind and P.S.Bataev [3], who showed that the ethers of tetraphenylbutynediol, in contrast to the glycol itself, did not add hydrogen at all in the presence of palladium or platinum. On the other hand, it differs somewhat from the observations made by Yu.S.Zalkind and I.Khazovaya [4] on the behavior of ethers of tetramethylbutynediol. In the presence of palladium the dimethyl ether of the latter is hydrogenated somewhat faster than the glycol itself, while its dibutyl ether is hydrogenated somewhat more slowly than the glycol.

TABLE 1

Time elapsed from start of hydrogenation, minutes	Methyl ether of methylbutynol		Methyl ether of methylbutenol
	Hydrogen added		
	% of 2H	% of 4H	% of 2H
5	34.0	17.0	13.6
10	59.0	29.5	20.0
15	68.8	34.4	–
20	73.4	36.7	28.9
30	79.0	39.5	35.9
40	82.2	41.1	40.9
70	89.2	44.6	52.6
110	97.6	48.8	62.6
140	101.0	50.5	68.0
200	–	54.5	77.2
260	–	56.1	84.0
320	–	57.6	–

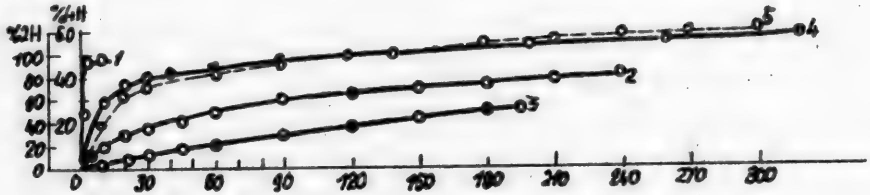


Fig. 1.

1-Methylbutenol; 2-methyl ether of methylbutenol; 3-methyl ether of methylbutenol plus 2 ml of thiocyanochlorobenzene; 4-methyl ether of methylbutynol; 5-methyl ether of methylbutynol plus 2 ml of thiocyanochlorobenzene.

We are inclined to attribute the marked inhibition of the hydrogenation of our ethers, compared to that of the alcohols themselves, to the same cause cited by Yu.S.Zalkind in the foregoing instances, namely steric hindrances, due to the substitution of methyl for hydrogen, which interferes with access to the carbon atoms attached to the triple or double bond.

These ethers were then hydrogenated with the three inhibitors we had previously employed in hydrogenating alcohols [1]: phenyl mustard oil, p-thiocyanochlorobenzene, and p-thiocyanoaniline. The latter slowed down the rate of hydrogenation here, too, but not as markedly as with the alcohols themselves (Figs. 1 and 2). Furthermore, the inhibition of the hydrogenation of the ethylenic ether proved to be greater than that of the acetylenic one, as before. The comparatively slight effect of the inhibitors upon the hydrogenation of the ethers, as against their effect on the alcohols, is evidently due to the fact that the very substituion of methyl for the alcohol's hydrogen causes a very considerable diminution in the rate of hydrogenation.

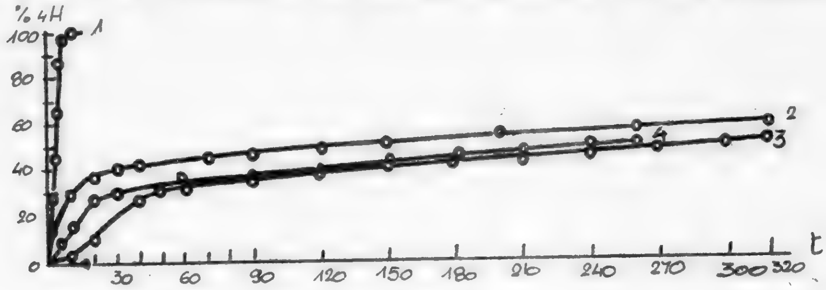


Fig. 2.

1-Methylbutynol; 2-methyl ether of methylbutynol; 3-methyl ether of methylbutynol plus 2 ml of phenyl mustard oil; 4-methyl ether of methylbutynol plus 2 ml of thiocyanoaniline.

EXPERIMENTAL

(V. A. Orestova and L. L. Chernekova)

The original alcohols were purified by repeated distillation into a column fitted with a worm condenser. The methylbutynol used had a b.p. of 103-105°, while that of the methylbutenol was 97-98°. Endeavors to secure the methyl ethers of methanol and of these alcohols by the use of various dehydrating substances (sulfuric acid, p-toluenesulfo acid, and sulfanilic acid) were not very successful. The best results were obtained by treating the alcoholates of these alcohols with methyl iodide.

Synthesis of the methyl ether of methylbutynol. 0.25 mole of methylbutynol and 100 ml of absolute ether were placed in a round-bottomed, three-necked flask, fitted with a stirrer and a reflux condenser. 0.25 g-atom of metallic sodium was added in small pieces, with constant stirring. The dissolution of all the sodium and the formation of an alcoholate required 6-8 hours. 0.35-0.4 mole of methyl iodide, with a b.p. of 43°, was poured into the resultant alcoholate at room temperature. Then the reaction mass was heated, with constant stirring, to 38-40° over a water bath for 14-16 hours. A precipitate of sodium iodide gradually settled out. The precipitate was suction-filtered, washed with ether, and desiccated. The filtrate was desiccated with potash and distilled into a column with a worm condenser. The yield of sodium iodide was 36.5 g (theoretically 37.5 g). The yield of the methyl ether of methylbutynol was 8.1 g (33% of the theoretical).

The ether exhibited a reaction with ammoniacal silver nitrate.

Percentage of methoxy groups by the Zeisel method: 30.6%; 31.6% computed. d_{20}^{20} 0.8052; n_D^{20} 1.4013; MR 29.59 (computed 29.55). B.p. 79-80°; freezing point -51-52°.

0.1308 g substance: 0.3506 g CO_2; 0.1246 g H_2O. Found %: C 73.10; H 10.58. $C_6H_{10}O$. Computed %: C 73.42; H 10.27. 0.2207 g substance: 18.43 g benzene; Δt 0.619°. Found: M 99.2; computed: M 98.1.

The ether was a mobile, colorless liquid with a pleasant odor. It is soluble in ethyl ether, benzene, and alcohol; it is insoluble in water.

Methyl ether of methylbutenol. This was synthesized exactly like the foregoing one, from methylbutenol. The reaction of the alcoholate with methyl iodide was much faster: 6-7 hours of heating over a water bath were enough, instead of 14-16 hours in the previous synthesis. The yield was 40-45% of the theoretical (26.5 g of the alcohol yielded 14 g of the ether). The yield of sodium iodide in this instance was 42.0 g instead of the 46.2 g called for theoretically.

The yield of the ethers can be increased by employing a better rectifying tower.

This ether was also a mobile, colorless liquid with a pleasant odor. It was soluble in ether, benzene, and alcohol, but insoluble in water. It decolorized bromine water rapidly.

Percentage of methoxy groups by the Zeisel method. 29.02%; computed 31.0%; b.p. 82-83°, freezing point -68°; d_{20}^{20} 0.7871; n_D^{20} 1.4008; MR_D 30.91; computed 31.08.

0.1066 g substance: 0.2800 g CO_2; 0.1144 g H_2O. Found %: C 71.63; H 11.92. $C_6H_{12}O$. Computed %: C 71.93; H 12.09. 0.1585 g substance: 17.57 g benzene: Δt 0.456°. Found M 101.3. Computed M 100.1.

The Chugaev-Tserevitinov reaction for hydroxy groups was negative.

Hydrogenation of the ethers. The hydrogenation conditions, the apparatus and the preparation of the colloidal Pd catalyst were the same as in our previous researches [1]. In the subjoined tables, t denotes the time elapsed from the start of the reaction, in minutes; P is the pressure; H_2 is the volume of hydrogen (in ml), on the basis of 2 hydrogen atoms per molecule of the substance being hydrogenated; $2H_2$ is the volume of hydrogen (in ml), on the basis of 4 hydrogen atoms per molecule of the acetylenic ether; V is the volume of hydrogen (in ml) absorbed since the start of the reaction; and v is the hydrogen volume absorbed since the previous reading. We checked each experiment by repeating it. We do not cite the results of our tests made to check the activity of the catalyst, using the hydrogenation of tetramethylbutynediol, methylbutynol, and methylbutenol with and without inhibitors, inasmuch as they agreed with our previous results.

Hydrogenation of the Methyl Ether of Methylbutynol

0.98 g of the ether (0.01 mole); 51 ml of ethyl alcohol; 3 ml (3 mg) of Pd; P 749.3 mm, T 20°; computed H_2 244.0 ml; $2H_2$ 488 ml.

t	5	10	20	40	70	110	140	200	320
v	83	61	35	22	17	20	8	20	15
V	83	144	179	201	218	238	246	266	281
% H_2	34.0	59.0	73.4	82.2	89.2	97.6	101	–	–
% $2H_2$	17.0	29.5	36.7	41.1	44.6	48.8	50.5	54.5	57.6

Hydrogenation of the Methyl Ether of Methylbutynol with Inhibitors

0.98 g of the ether (0.01 mole); 50 ml of ethyl alcohol; 2 ml (0.4 mg) of phenyl mustard oil; 3 ml (3 mg) Pd; P 769.4 mm, T 20°; computed H_2 238.0; $2H_2$ 476 ml.

t	10	20	30	60	120	180	240	330
v	12.5	36.5	67	40	28	20	17	20
V	12.5	49	116	156	184	204	221	241
% H_2	5.2	19.6	48.6	65.4	77.2	85.6	92.8	101.2
% $2H_2$	2.6	9.8	24.3	32.7	38.6	42.8	46.4	50.6

Hydrogenation of the Same Ether Under the Same Conditions, but with 2 ml (0.4 mg) of p-Thiocyanochlorobenzene

t	10	20	30	60	120	180	240	285
v	90	61	18	31	34	23	19	9
V	90	151	169	200	234	257	276	285
% H_2	37.4	63.4	71.0	85.0	98.2	–	–	–
% $2H_2$	18.7	31.7	35.5	42.5	49.1	53.9	57.9	59.9

Hydrogenation of the Same Ether Under the Same Conditions, but with 2 ml (0.4 mg) of p-Thiocyanoaniline

t	10	20	30	60	120	180	240	255
v	72	64	8	19	28	20	20	4
V	72	136	144	163	191	211	231	235
% H_2	30.2	57.0	60.4	68.4	80.0	88.4	96.8	98.6
% $2H_2$	15.1	28.5	30.2	34.2	40.0	44.2	48.4	49.3

Hydrogenation of the Methyl Ether of Methylbutenol

1.0 g of the ether (0.01 mole); 51 ml of ethyl alcohol; 3 ml (3 mg) of Pd; P 757.2 mm; T 20°; computed. H_2 242.0 ml.

t	5	10	20	30	60	120	180	240
v	33	16	21	17	34	36	23	18
V	33	49	70	87	121	157	180	198
% H_2	13.6	20	28.9	35.9	50.0	64.9	74.4	81.8

Hydrogenation of the Same Ether with an Inhibitor

1.0 g of the ether (0.01 mole); 50 ml of ethyl alcohol; 2 ml (0.4 mg) of p-thiocyanochlorobenzene; 3 ml (3 mg) of Pd; P 758.0 mm; T 20°; computed. H_2 241.0 ml.

t	10	20	30	60	120	180	240
v	4	8	8	18	31	33	30
V	4	12	20	38	69	102	132
% H_2	1.7	4.8	8.3	15.8	28.6	42.4	54.8

SUMMARY

The methyl ethers of methylbutynol and methylbutenol have been synthesized and their properties described. It has been shown that the hydrogenation of these ethers with colloidal palladium is much slower than the hydrogenation of their alcohols, owing to the methyl group's screening of the triple or double bond.

The inhibitory effect of certain substances – phenyl mustard oil, p-thiocyanoaniline, and p-thiocyanochlorobenzene – on the hydrogenation of these ethers with colloidal palladium has been established.

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THE SYNTHESIS AND STRUCTURE OF SOME DERIVATIVES OF COLCHICINE

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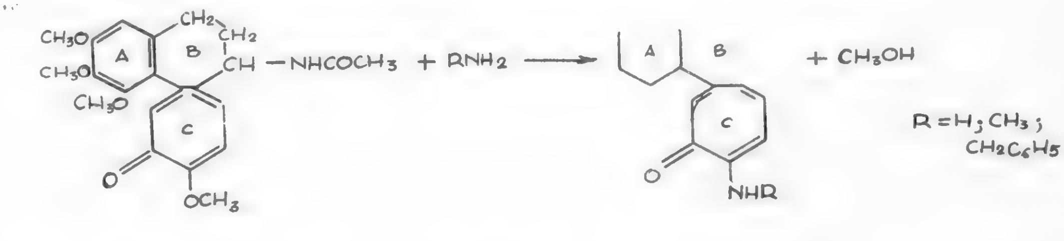
Most of the known researches on colchicine, devoted to establishing its structure, describe derivatives of colchicine, produced by a more or less far-reaching cleavage of the latter's molecule and representing one or another product of its decomposition.

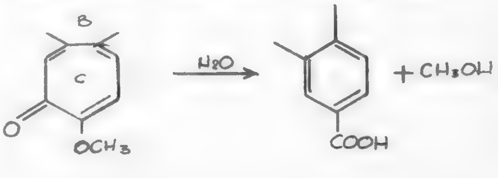
We set ourselves the task of synthesizing new colchicine compounds by introducing substituents without rupturing the basic skeleton of the colchicine molecule. We started by synthesizing amino derivatives of colchicine.

As far back as 1888, Zeisel [1] described the product obtained by substituting an amino group for the ether grouping in the third colchicine ring and called it colchiceineamide. This substance, prepared by heating colchicine to 100° with an alcoholic solution of ammonia, occurred as yellowish crystals that had the composition of $C_{21}H_{24}N_2O_5 \cdot \frac{1}{5} C_2H_5OH$ after recrystallization from alcohol. No other data was furnished. The synthesis of some alkyl amines of this type is described in the patent issued to Ewins and Ashley [2].

We prepared amino derivatives of colchicine by reacting ammonia or amines with colchicine directly in alcoholic solution at temperatures ranging from 100 to 160° We synthesized aminocolchiceine, methylaminocolchiceine, diethylaminocolchiceine, and benzylaminocolchiceine. Carbethoxyaminocolchiceine (colchicine urethane) was synthesized by us by the Claisen method [3], the dissolved base reacting with ethyl chlorocarbonate in the presence of powdered potash. Under the conditions employed, ammonia and the other amines react without rupturing the structure of Ring C of colchicine (which has been recently shown to be a seven-membered ring [4]), the reaction involving substitution of an amino group for the ether group:



This is borne out by the nature of the absorption spectra of aminocolchiceine and methylaminocolchiceine, which retain the two maxima at 2400 and 3600 A that are characteristic of colchicine, together with a new maximum at 4100. The action of an alcoholic solution of an alcoholate upon colchicine is quite different, causing saponification of the methoxy group in the seven-membered Ring C, together with



aromatization of the ring and the formation of an acid, called colchicinic acid, even when it is allowed to stand with the colchicine at room temperature, while the reaction proceeds more rapidly when the mixture is heated to 100°. When this reaction is carried out in the presence of an alkyl halide, we get esters of colchicinic acid.

The transformation occurring during this reaction may be classified as a benzyl rearrangement; it is typical of such seven-membered structures, for example, purpurogallin, as has been recently proved by Barltrop and Nicholson [5].

Study of the absorption spectra of colchicinic acid and of its esters likewise indicates that the structural changes in the colchicine molecule are more farreaching than when the latter is acted upon by alcoholic ammonia. The shape of the absorption curve changes, becoming simpler, as it were; the maxima that are characteristic of colchicine vanish, a new maximum appearing at 2800 A. A spectrum of this sort bears out the assumption that the seven-membered Ring C has been aromatized, since it is typical of a trimethoxy-substituted biphenyl derivative. This is seen from the following comparison: trimethyl-pyrogallol has an absorption band at 2750 A with an intensity of $\ln \underline{k} = 2.8$; the introduction of another aromatic ring with a carboxyl group ought to shift the absorption maximum toward the longer wavelengths and increase the absorption intensity considerably, as is usually the case when we turn from benzene derivatives to derivatives of biphenyl [6,7].

During the preparation of our paper for publication, a paper by Santavy [8] has been published in which the author endeavors, like us, to synthesize N-methylcolchicine, the formation of which by the action of sodium alcoholate and methyl iodide upon colchicine was indicated by Zeisel [9], without however, giving any constants for this compound. Santavy secured colchicinic acid and converted it into its methyl ester by means of diazomethane.

EXPERIMENTAL

Aminocolchiceine. 1 g of colchicine and 1.5 ml of 5% alcoholic ammonia were heated together to 100° in a sealed tube for 4 hours. The color of the solution gradually changed from an initial wine-yellow to brown, and by the end of the third hour of heating large crystals settled out, more of them appearing as the solution cooled. The crystals were filtered out and washed with ether. Yield: 0.64 g. Another 0.12 g of the substance was recovered from the mother liquor by adding absolute ether to it. Recrystallization from a mixture of benzene and (15%) alcohol yielded 0.5 g of the amine as light-yellow crystals with a m.p. of 260-262° (darkening at 258°). Aminocolchiceine is readily soluble in chloroform, acetone, and alcohol, but sparingly soluble in ether. Its solubility in water is about 0.1%; the aqueous solution has a pH of 7.8.

0.0492 g substance in 5 ml chloroform; $\underline{l}$ 0.5 dm; α -0.71°; $[\alpha]_D$ -144.31°.

6.437 mg substance: 0.392 ml N_2 (22°, 728.5 mm). 5.971 mg substance: 0.3636 ml N_2 (21°, 733.5 mm). Found %: N 6.76, 6.82.
$C_{21}H_{24}O_5N_2 \cdot {}^1/_2 C_2H_5OH$. Computed %: N 6.89.

Methylaminocolchiceine. 0.5 g of colchicine was dissolved in 0.75 ml of ethyl alcohol, and 2.23 ml of a 10% alcoholic solution of methylamine was added. The sealed tube was set aside to stand for three days at room temperature. The solvent was evaporated in vacuum in the cold. The substance slowly settled out from a dilute ether solution (to which 2% alcohol had been added) as yellow crystals. Yield: 0.3 g; m.p. 172-178°. Methylaminocolchiceine is readily soluble in alcohol, chloroform, and acetone; it is sparingly soluble in water. The pH of a 0.1% aqueous solution was 6.6.

0.0342 g substance in 5 ml chloroform; l 0.5 dm; α -0.56°; $[\alpha]_D$ -160.82°.

4.125 mg substance: 0.255 ml N_2 (22°, 740.5 mm). 4.293 mg substance: 0.269 ml N_2 (22°, 741.0 mm). Found %: N 6.97, 7.07. $C_{22}H_{26}N_2O_5$. Computed %: N 7.03.

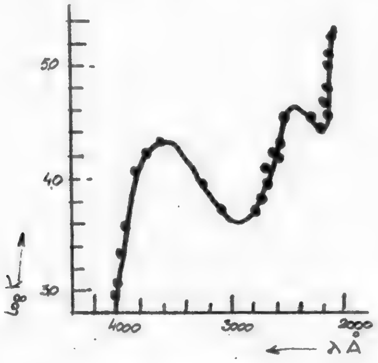


Fig. 1. Colchicine

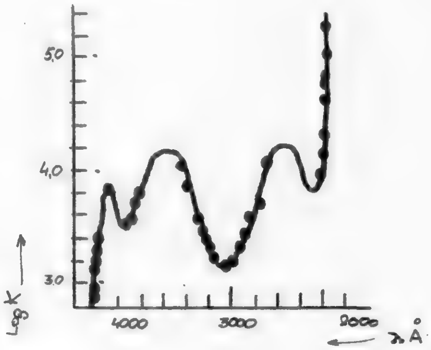


Fig. 2. Aminocolchiceine

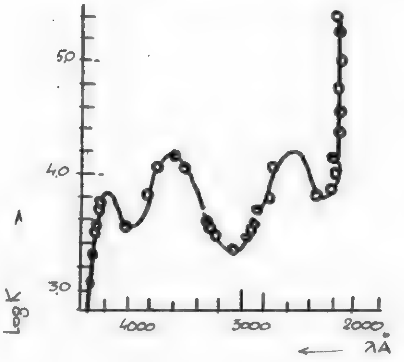


Fig. 3. Methylamino-colchiceine

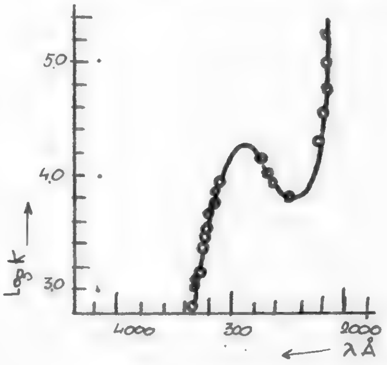


Fig. 4. Ethyl ester of colchicinic acid

Ultraviolet absorption spectra (solutions in ethyl alcohol)

Diethylaminocolchiceine. 1 g of colchicine and 1 g of freshly distilled diethylamine were heated together for 2.5-3 hours in a sealed tube over a water bath. When the reaction mass cooled, a large quantity of big, lustrous crystals settled out. The crystals were filtered out and washed with ether. Recrystallization from acetone to which a drop of alcohol (2-3%) had been added yielded minute, bright-yellow crystals with a m.p. of 208-209°. Yield: 0.5 g. Diethylaminocochiceine is freely soluble in benzene and alcohol, somewhat less freely in ether and acetone, and sparingly in water.

0.0509 g substance in 5 ml chloroform: l 0.5 dm; α +2.66°; $[\alpha]_D$ + 521.62°.

7.324 mg substance: 3.30 ml 0.01 N H_2SO_4. 7.818 mg substance: 3.52 ml 0.01 N H_2SO_4. Found %: N 6.31, 6.30. $C_{25}H_{82}N_2O_5$. Computed %: N 6.36.

Benzylaminocolchiceine. 0.5 g of colchicine and 0.4 g of benzylamine were heated together in 3.3 ml of alcohol for 6 hours in a sealed tube over a water bath. The excess amine and solvent were driven off in vacuum in the cold. The substance, which dried out as a film, was triturated with absolute ether and carefully washed with the latter. The substance was washed with water to remove any traces of colchicine. The residue was dissolved in absolute alcohol and filtered, and the solvent was again driven off in vacuum. The softening point was 120-124° after drying to constant weight. Yield: 0.3 g. Benzylaminocolchiceine is a bright-yellow powder; it is freely soluble in alcohol, acetone, and chloroform, less freely in ether, and very slightly soluble in water. The pH of a 0.05% aqueous solution was 7.0.

0.0414 g substance in 5 ml chloroform; $\underline{l}$ 0.5 dm; α -0.51°; $[\alpha]_D$ -123.18°.

7.352 mg substance: 3.08 ml 0.01 $\underline{N}$ H_2SO_4. 7.445 mg substance: 3.09 ml 0.01 $\underline{N}$ H_2SO_4. Found %: N 5.86, 5.81. $C_{28}H_{30}N_2O_5$. Computed %: N 5.90.

Carbethoxycolchiceine. 0.6 g of ethylchlorocarbonate was added with constant stirring and heating to 0.85 g of aminocolchiceine and 1.2 g of freshly calcined potash in 30 ml of dioxane. Then the reaction mixture was heated to 80-85° for 8 hours, with constant stirring. The inorganic precipitate was filtered out, dissolved in hot water and subjected to a Volhard titration. The quantity of chlorine found indicated that 95% of the ethyl chlorocarbonate used entered into the reaction. The solvent was driven off in vacuum, and the solid residue was dissolved in a 1:2 chloroform:ether mixture and analyzed chromatographically in a column filled with 22 g of alumina, from which the alkali had been washed out by the Carter method.[6] The substance was removed from the alumina with alcohol (6 batches of 25 ml each), the alcohol was driven off in vacuum, and the residue was evaporated in vacuum in the cold. Yield: 0.66 g. Carbethoxyaminocolchiceine is an amorphous, bright-yellow powder with a softening point at 112-120°. It is sparingly soluble in ether, petroleum ether, benzene, and water, but very soluble in alcohol and acetone.

0.0598 g substance in 5 ml chloroform; $\underline{l}$ 0.5 dm; α -0.76°; $[\alpha]_D$ -127.09°.

6.979 mg substance: 0.382 ml N_2 (19.5°, 743 mm). Found %: N 6.25. $C_{24}H_{28}N_2O_7$. Computed %: N 6.13.

Methyl ester of colchicinic acid. 1 g of colchicine was heated in a sealed tube to 100° for 4 hours with an alcoholate solution, prepared with 0.1 g of metallic sodium in 5 ml of absolute alcohol. The solvent was driven off in vacuum in the cold. The dry residue was reheated with 10 g of methyl iodide to 100° in a sealed tube for 4 hours. The methyl iodide was driven off, and the substance was treated with hot water, the insoluble bulk of the substance then being twice recrystallized from 15 times its weight of absolute alcohol. Yield 0.5 g. The methyl ester of colchicinic acid consists of colorless crystals with a m.p. of 254-255°. They are soluble in alcohol and chloroform, but practically insoluble in water. Saponification with an alcoholic alkali yields colchicinic acid.

0.0534 g substance in 5 ml chloroform. $\underline{l}$ 0.5 dm; α -0.71°; $[\alpha]_D$ -132.71°.

4.166 mg substance: 10.109 mg CO_2; 2.340 mg H_2O. 4.078 mg substance: 9.899 mg CO_2; 2.33 mg H_2O. 7.515 mg substance: 0.231 ml N_2 (21°, 738 mm). 7.887 mg substance: 0.247 ml N_2 (22°, 733 mm). Found %: C 66.18, 66.20; H 6.20, 6.32; N 3.47, 3.48. $C_{22}H_{25}O_6N$. Computed %: C 66.15; H 6.28; N 3.52.

Colchicinic acid. 1 g of colchicine was heated in a sealed tube for 4 hours to 100° with an alcoholate solution prepared with 0.1 g of metallic sodium in 5 ml of absolute methanol. The solvent was driven off in vacuum in the cold. The solid residue was dissolved in 10 ml of water. When the solution was acidified with a 1% solution of hydrochloric acid, the colchicinic acid settled out as a copious gray precipitate, which was filtered out and washed with water. Colorless crystals of the substance, with a m.p. of 257-258° were secured after two recrystallizations from 1:1 aqueous alcohol and one recrystallization from acetone. Colchicinic acid is very slightly soluble in water, but soluble in a 1% solution of sodium bicarbonate; it titrates with 1 equivalent of alkali. The yield of the substance was 0.6 g.

Ethyl ester of colchicinic acid. 2 g of colchicine was heated in a sealed tube for 4 hours to 100° with a solution of alcoholate, made from 0.2 g of metallic sodium and 8 ml of absolute methanol. The solvent was driven off in vacuum in the cold, and the solid residue (the sodium salt of colchicinic acid) was heated in a sealed tube to 100° for 4 hours with an excess (15 g) of ethyl iodide. The ethyl iodide was then driven off, and the solid residue was treated with hot water. The bulk of the residue ($\sim$ 1.5 g), which was insoluble in water, was dissolved in 100 ml of a chloroform-ether mixture and chromatographed through a column containing 22 g of alumina, washed free of alkali by the Carter method. The top layer of the alumina, containing tar, was discarded, and the substance was extracted from the alumina with alcohol (7 batches of 25 ml each). The alcohol was driven off in vacuum. Yield: 0.6 g. The substance was recrystallized twice from a mixture of alcohol with 20% of ether. This yielded 0.3 g of the ethyl ester of colchicinic acid, with a m.p. of 217°. The substance is sparingly soluble in water and ether, but very soluble in alcohol and acetone. Saponification of the ethyl ester with an alcoholic alkali yielded colchicinic acid with a melting point of 255° after crystallization from acetone, which exhibited no depression when the melting point of a test sample mixed with the previously prepared colchicinic acid was determined.

0.0546 g substance in 5 ml chloroform: $\underline{1}$ 0.5 dm; α -0.73°; $[\alpha]_D$ -133.7°.

3.572 mg substance: 8.782 mg CO_2; 2.090 mg H_2O. 6.315 mg substance: 0.192 ml N_2 (24.5°, 730.5 mm). 8.002 mg substance: 0.238 ml N_2 (22.5°, 725.5 mm). Found %: C 67.05; H 6.55; N 3.35, 3.28.
$C_{23}H_{27}O_6N$. Computed %: C 67.03; H 6.55; N 3.39.

SUMMARY

A study has been made of the reaction of colchicine with alcoholic solutions of organic amines and with an alcoholic solution of sodium alcoholate; it was found that in the former cases the methoxy group in Ring C is replaced by amino groups, while in the latter case, this methoxy group is saponified, the Ring C is aromatized, and a salt of colchicinic acid is formed.

The ethyl and methyl esters of this acid, synthesized by reacting alkyl halides with its salts, have been described.

Carbethoxyaminocolchiceine has been synthesized by reacting aminocolchiceine with ethyl chlorocarbonate.

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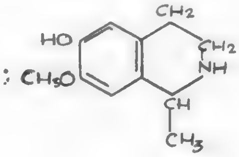
THE ALKALOIDS OF SALSOLA RICHTERI

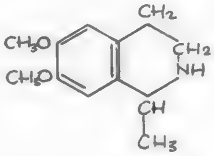
VI. THE N-DERIVATIVES OF SALSOLINE. II

N. F. Proskurnina and V. M. Merlis

In our preceding report on the alkaloids of Salsola Richteri (Report V) [1], we described the synthesis of several derivatives of salsoline (I) and salsolidine (II).



(I)



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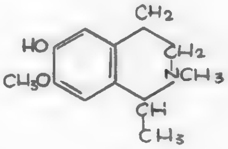


(III)

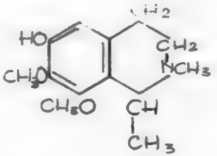
Continuing our research along these lines, we synthesized r-N-methylsalsoline (III) by heating r-salsoline with formaldehyde in the presence of formic acid, by the Wallach method [2].

When we methylated optically active salsoline by this same method, we made the following interesting observation: we got the same r-N-methylsalsoline instead of the expected optically active N-methylsalsoline. Thus, under these conditions the reaction product is racemized.

To ascertain the causes of this racemization of N-methylsalsoline, we attempted to prepare optically active N-methylsalsoline by methylating salsoline with methyl iodide. Our experiment failed to yield N-methylsalsoline. The methiodide of N-methylsalsoline, which proved to be the principal reaction product, was likewise optically inactive. Thus, even under the mild conditions under which methylation takes place with methyl iodide the reaction product is racemized. We may therefore infer that N-methylsalsoline displays an extremely great tendency toward racemization, whereas the initial salsoline does not possess this property.

In fact, numerous attempts to racemize optically active salsoline were fruitless, despite the severe conditions employed, e.g., heating with strong acids or an alcoholic alkali as well as heating its salts to high temperatures. Some of the experiments on racemizing optically active salsoline that met with failure are cited in the present paper.

E. Späth and F. Kesztler [3] also observed the extraordinarily high tendency of pellotine (IV), which belongs to the same series of tetrahydroisoquinoline alkaloids, toward racemization. These authors attribute this property of pellotine to its possessing a phenyl group.



(IV)

In support of this hypothesis, E. Späth and

F.Dengal [4] point out the high resistance of salsolidine, which is not a phenolic base, to racemization. Their attempts to racemize optically active salsolidine were unsuccessful, and when they methylated d-salsolidine with formaldehyde and formic acid, they secured d-N-methylsalsolidine.

Even earlier, the resistance of salsolidine to racemization was noted by N. Proskurnina and A.Orekhov [5], who methylated l-salsolidine with methyl iodide and secured an optically active methiodide with the sign of rotation merely reversed.

When we compare all these facts, the conclusion asserts itself that the alkaloids of this series possess a pronounced tendency toward racemization only when their molecules contain both the phenol and methylimido groups, as may be seen by inspection of the pellotine and the N-methylsalsoline.

It is interesting to trace this rule in other N-substituted derivatives of salsoline.

EXPERIMENTAL

Methylation of r-salsoline with formaldehyde and formic acid. 3 g of formaldehyde and 2 g of formic acid were added to 5.65 g of r-salsoline, with a m.p. of 218°. Bubbles of CO_2 began to evolve at once. The solution was heated for 2.5 hours over a water bath, and then saturated with potash and extracted with ether. Driving off the ether yielded 5.1 g of a base, which was dissolved in a small amount of alcohol. Adding alcoholic HCl threw down a precipitate. Suction filtering, washing with acetone, and recrystallizing from alcohol yielded 5.2 g of the hydrochloride with a m.p. of 236-237°.

0.1405 g substance: 5.7 ml 0.1 N $AgNO_3$. Found %: Cl 14.4.
$C_{12}H_{17}NO_2 \cdot HCl$. Computed %: Cl 14.58.

The crystalline base recovered from the hydrochloride had a m.p. of 143° after recrystallization from alcohol.

4.221 mg substance: 0.252 ml N_2 (26°, 749 mm). Found %: N 6.55.
$C_{12}H_{17}NO_2$. Computed %: N 6.76.

Hydriodide. HI was added to an alcoholic solution of the base. The precipitate that settled out upon trituration with acetone had a m.p. of 202-203° after recrystallization from alcohol.

Hydrobromide. HBr was added to an alcoholic solution of the base. The precipitate that settled out when the alcohol was evaporated was washed with acetone. The hydrobromide did not melt though heated to 300°, after having been recrystallized from alcohol.

Methylation of d-salsoline with formaldehyde and formic acid. 2 g of formaldehyde and 1.5 g of formic acid were added to 4.2 g of d-salsoline, prepared from the hydrochloride, with $[\alpha]_D + 38.3$. The solution was heated for 2.5 hours and then saturated with potash and extracted with ether. The ether was driven off, and the base recovered by adding alcoholic HCl; it was then converted into the hydrochloride, which had a m.p. of 236-237° after having been recrystallized from alcohol. A test sample, mixed with the hydrochloride of r-N-methylsalsoline, exhibited no depression of the melting point. The hydrochloride was optically inactive. The base recovered from the hydrochloride had a m.p. of 143° after crystallization from alcohol. A test sample, mixed with methylsalsoline, exhibited no depression of the melting point.

Methylation of d-salsoline with methyl iodide. 0.8 g of d-salsoline, with a m.p. of 213-215°, recovered from the hydrochloride, with a specific rotatory power of $[\alpha]_D +38.8°$, was dissolved in 53 ml of methanol, and 3 ml of methyl iodide was added. The mixture was heated for 30 minutes over a water bath, after which the methanol was driven off, and the semiliquid residue was placed in a vacuum desiccator. The dark-yellow crystallized mass was washed with acetone. Two recrystallizations from alcohol yielded 0.5 g of a white crystalline substance with a m.p. of 232-234°. The synthesized methiodide was optically inactive. It was readily soluble in water and in dilute NaOH. Unreacted d-salsoline was recovered from the mother liquor.

Attempts to racemize optically active salsoline. 1.3 g of d-salsoline hydrochloride, with a specific rotatory power of $[\alpha]_D + 34.5°$, was heated to 175° for 5 hours. The rotatory power remained unchanged.

2.5 g of d-salsoline, recovered from the hydrochloride, with a specific rotatory power of $[\alpha]_D +34,5°$, was boiled with 40 ml of a 10% alcoholic solution of KOH for 5 hours. The alkaline solution was acidified with HCl, the precipitated hydrochloride was suction-filtered out and washed with acetone. Its specific rotatory power was $[\alpha]_D +34.4°$.

SUMMARY

1. Methylation of optically active salsoline with formaldehyde and formic acid yields racemic N-methylsalsoline.

2. Methylation of optically active salsoline with methyl iodide yields a racemic methiodide of N-methylsalsoline.

3. Previous observations concerning salsoline's resistance to racemization have been confirmed.

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XXXII. CHROMIC OXIDE ON ALUMINA AS A CATALYST FOR CONVERSIONS OF HETEROCYCLIC COMPOUNDS

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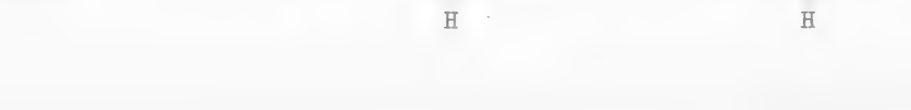
The present paper reports on a study of a mixed catalyst – chromic oxide on alumina – in the conversion of furanidine (tetrahydrofuran) into pyrrolidine and thiophane. This catalyst, widely used of late to aromatize paraffins, dehydrogenate cycloparaffins, and isomerize diolefins, was prepared by one of the common methods employed for its manufacture; the samples of catalyst contained 9.5, 14, 20.2, and 33.5% chromic oxide. A catalyst with the following composition: 12% chromic oxide and 88% alumina, was used to repeat the transformation of α-methylfuran and α-methylfuranidine into α-methylpyrrole and α-methylpyrrolidine, respectively, described by one of the present authors; the data cited in the paper referred to [2] merely corroborated the results achieved by us earlier.

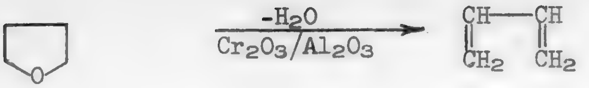
In the present paper we have demonstrated that none of the tested samples of chromic oxide on alumina produced as high yields of pyrrolidine or thiophane as had been produced with alumina alone in the conversion of furanidine into pyrrolidine or in the conversion of furanidine into thiophane.

The optimum temperature for the conversion of furanidine into pyrrolidine is 350°. The conversion of furanidine into pyrrolidine exhibited a specific peculiarity of chromic oxide on alumina as a dehydrogenation catalyst: in the 350-500° range, pyrrole was produced in addition to pyrrolidine, the quantities of the former being much larger than was the case when the reaction was carried out with alumina. The pyrrole yield was 17% of the theoretical (400°; 33.5% Cr_2O_3). The optimum temperature for dehydrogenating the pyrrolidine formed was 400°; the pyrrole yield dropped off as the temperature was raised still higher.

At 400°, perceptible amounts of carbazole appeared in the catalyzates. As the temperature was raised beyond this point, the amount of carbazole increased, its yield being 22% of the theoretical at 500° (a catalyst containing 20.2% Cr_2O_3) The formation of carbazole may be a result of the following series of reactions: the action of ammonia upon furanidine in the presence of chromic oxide upon alumina converted the latter into pyrrolidine, which was catalytically dehydrogenated into pyrrole (I); the transformation into pyrrolidine was paralleled by the dehydration of the furanidine into butadiene-1,3 (II); condensation of two molecules of butadiene with one molecule of pyrrole at high temperature split out hydrogen and formed carbazole (III):



(I)



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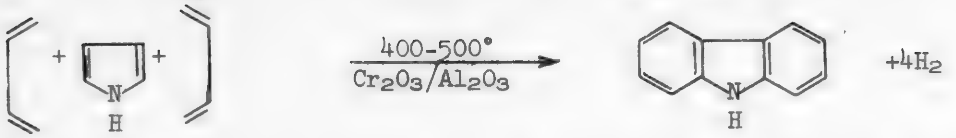
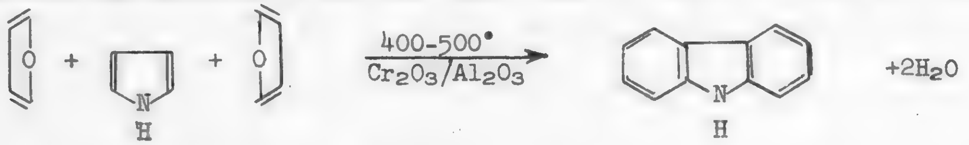


(III)

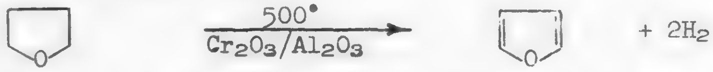
Another process is conceivable for the formation of carbazole: dehydrogenation of furanidine above Cr_2O_3/Al_2O_3 yielded furan, two molecules of which condensed with one molecule of pyrrole (splitting out water) to form the carbazole:



It is not impossible that the reaction followed this latter course,* but it seemed less likely because furanidine, in contrast to pyrrolidine [3] and thiophane [4], was not dehydrogenated even by very active samples of a Pt/charcoal catalyst, neither at 350° [5] nor at 400° [6].

In our present research, however, we have effected the catalytic dehydrogenation of furanidine. When we passed furanidine over Cr_2O_3/Al_2O_3 (20.2% Cr_2O_3) at 500°, we secured a small quantity of furan, though the bulk of the catalyzate consisted of high-boiling compounds (b.p. up to 260°). That portion of the catalyzate was, no doubt, a product of the polymerization of the dihydrofuran formed during the step-by-step dehydrogenation of the furanidine. The high percentage of hydrogen in the gas evolved during the experiment (59%) was likewise evidence that the furanidine had been dehydrogenated catalytically.

Thus, in our present research, furanidine has been catalytically dehydrogenated to furan for the first time:



The dehydrogenation of the furanidine was paralleled by its dehydration, yielding butadiene-1,3, which constituted 6% of the exhaust gases. We also observed the decomposition of the furanidine to propylene [7], which is usual whe oxide catalysts are employed.

The presence of furan and butadiene in the products of the catalysis of furanidine above chromic oxide on alumina at 500° justifies the assumption that carbazole can be formed in both of the ways cited above.

No dehydrogenation of the thiophane was observed when furanidine was converted into thiophane above chromic oxide on alumina at 250-400°. This may be due to the fact that thiophane is dehydrogenated in the presence of platinized charcoal only at 350-400° [4], and even then not completely, so that its dehydrogenation above Cr_2O_3/Al_2O_3 would have required a higher temperature than that needed for the dehydrogenation of pyrrolidine. Pyrrolidine is completely dehydrogenated to pyrrole at 300° in the presence of platinized asbestos [3]

EXPERIMENTAL

Each set of tests was made with the same sample of catalyst, with subsequent regeneration of the latter.

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*A reaction of this type has been described for the formation of indole from two molecules of pyrrole [12] ammonia being split out. Hence, the formation of carbazole may also be thought of as the result of the condensation of three molecules of pyrrole, two molecules of ammonia being split out.

1. Conversion of Furanidine into Pyrrolidine, Pyrrole, and Carbazole

The furanidine was passed over the catalyst in a current of ammonia at the rate of 6-7 drops per minute. The rate of feed of the ammonia was the same in each test, being set at the optimum value. The tests were run at 300, 350, 400, 450, and 500°. The receiver and the worm-condenser trap attached to it were well chilled. The resulting condensate was saturated with caustic soda, and the oily layer was separated and desiccated with fused caustic soda. An excess of the solid alkali was added to the aqueous solution, and then the latter was distilled into a dephlegmator, collecting the fraction that passed over up to 100°. This fraction was combined with the oily part of the condensate, and then the mixture of the reaction products was carefully desiccated and distilled.

The pyrrolidine and pyrrole were isolated by distillation; the carbazole was collected at the end of the reaction tube and from the receiver, some of it also being recovered from the residues left after the pyrrolidine and the pyrrole had been driven off. During the first distillation, pyrrolidine was collected in the 85-89° range, and pyrrole in the 128-132° range.

The quantities (in grams) of nitrogenous products of the conversion of furanidine when it was acted upon by ammonia in the presence of various samples of chromic oxide upon alumina are given in Table 1. The yields of pyrrolidine, pyrrole, and carbazole are listed in Table 2, which also gives comparative data on the production of pyrrolidine with alumina alone.

Table 2 shows that when chromic oxide on alumina is used, the maximum yield of pyrrolidine was only 17.5-17% of the theoretical at 300-350°, whereas the yield of pyrrolidine was 30.5% of the theoretical [8] at 350° and 46.5% of the theoretical [9] at 400° over alumina alone. At these temperatures even the overall yield of nitrogenous products of the conversion of furanidine when Cr_2O_3/Al_2O_3 was used was lower than the yield of pyrrolidine alone when alumina was used.

The pyrrolidine secured in all the tests was combined; it possessed the following constants after redistillation:

B.p. 85.5-86.6° (751 mm); n_D^{20} 1.4431, d_4^{20} 0.8585; picrate (from alcohol), m.p. 112°; a test sample, mixed with pyrrolidine picrate, exhibited no depression.

Literature data: B.p. 85.4-86.4° (748 mm); n_D^{20} 1.4428; d_4^{20} 0.8576 [9].

The pyrrole combined from the various distillates had the following constants after another redistillation:

B.p. 130-131° (761 mm); n_D^{20} 1.5060; d_4^{20} 0.9502.

Literature data: B.p. 128.5° (746 mm); n_D^{21} 1.5093 [3]; B.p. 130-131° (760 mm); n_D^{20} 1.5091; d_4^{20} 0.9480 [10].

The carbazole had a m.p. of 236° after recrystallization from chloroform. A test sample, mixed with known carbazole, exhibited no depression.

Found %: N 8.36. $C_{12}H_9N$. Computed %: N 8.37.

2. Conversion of Furanidine Into Thiophane

The furanidine was passed over the catalyst in a current of hydrogen sulfide at the rate of 10-12 drops per minute. The condensate was saturated with caustic soda, and the reaction product was separated, desiccated with calcium chloride, and distilled in the 116-120° range into a dephlegmator above pieces of cuastic soda. No thiophene was found in the distillate. The results of our experiments on the conversion of furanidine into thiophane in the presence of chromic oxide on

Table 1

Reaction of furanidine with Ammonia in the Presence of Chromic Oxide on Alumina

Catalyst	9.5% Cr_2O_3				14% Cr_2O_3				20.2% Cr_2O_3				33,5% Cr_2O_3			
		g. of product				g. of product				g. of product				g. of product		
Temp.	Furanidine used g	Pyrrolidine	Pyrrole	Carbazole	Furanidine used g	Pyrrolidine	Pyrrole	Carbazole	Furanidine used g	Pyrrolidine	Pyrrole	Carbazole	Furanidine used g	Pyrrolidine	Pyrrole	Carbazole
300	10	0.3	0	0	10	0.55	Traces	0	15	2.6	Traces	0	15	2.0	Traces	0
350	10	0.4	Traces	0	10	0.5	1.0	0	15	2.5	0.7	0	15	2.4	1.5	0
400	10	0.3	0.25	0	10	0.65	0.5	0.1	15	0.7	1.4	0.4	15	1.0	2.4	0.3
450	10	0	0.1	Traces	10	0.3	0.35	0.3	15	0	1.0	0.7	15	0	1.6	0.9
500	10	0	Traces	0.15	10	0	0.25	0.25	15	0	0.75	2.6	15	0	0.9	1.4

Table 2

Yield of Nitrogenous Products in the Conversion of Furanidine with Chromic Oxide on Alumina (% of the theoretical)

Catalyst	9.5% Cr_2O_3			14% Cr_2O_3			20.2% Cr_2O_3			33.5% Cr_2O_3			Al_2O_3
Temp.	Pyrrolidine g	Pyrrole g	Carbazole g	Pyrrolidine g	Pyrrole g	Carbazole g	Pyrrolidine g	Pyrrole g	Carbazole g	Pyrrolidine g	Pyrrole g	Carbazole g	Pyrrolidine g
300	3.0	0	0	5.5	Traces	0	17.5	Traces	0	13.5	Traces	0	Slight
350	4.0	Traces	0	5.0	10.5	0	17.0	5.0	0	16.0	10.5	0	30.5 [8]
400	3.0	2.5	0	6.5	5.0	1.0	4.5	10.0	3.5	6.5	17.0	2.5	46.5 [9]
450	0	1.0	Traces	3.0	3.5	3.5	0	7.0	6.0	0	11.5	7.5	14.0 [8]
500	0	0	2.0	0	2.5	3.0	0	5.0	22.0	0	6.5	12.0	Not carried out

Table 3

Conversion of Furanidine into thiophane in the Presence of Chromic Oxide on Alumina

Catalyst	9.5% Cr_2O_3		14% Cr_2O_3		20.2% Cr_2O_3		33.5% Cr_2O_3		Thiophane yield (% of theoretical)				
Temp.	Furanidine used g	Thiophane yield g	Furanidine used g	Thiophane yield g	Furanidine used g	Thiophane yield g	Furanidine used g	Thiophane yield g	Al_2O_3	9.5% Cr_2O_3	14% Cr_2O_3	20.2% Cr_2O_3	33.5% Cr_2O_3
250	5.0	2.4	5.0	2.7	10	3.2	5.0	2.5	48.0	39.0	44.0	26.0	41.0
300	5.0	4.0	5.0	4 2	7.0	6.6	5.0	3.0	80.0	65.5	70.0	78.0	49.0
350	5.0	3.2	5.0	2.5	5.0	3.2	5.0	2.6	85.0	52.0	41.0	52.0	42.5
400	5 0	2.0	5.0	2.4	7.0	2.0	5.0	2.5	90.5	32.5	39.0	23.0	41.0

alumina are listed in Table 3. We see from this table (which also lists data on the production of thiophane in the presence of alumina alone) that 300° is the optimum temperature for converting furanidine into thiophane above chromic oxide on alumina (the thiophane yield being 78% of the theoretical). Nevertheless, the yield of thiophane was lower than the yield secured with alumina alone, at this optimum temperature as well as at all the others.

All the thiophane collected in all the tests was combined and redistilled above sodium, after which it had the following constants:

B.p. 119.5-120° (760 mm); n_D^{20} 1.5050; d_4^{20} 0.9959.

Literature data: B.p. 119.8-120° (760 mm), n_D^{20} 1.5052; d_4^{20} 0.9960 [8].

3. Behavior of Funanidine in the Presence of Cr_2O_3/Al_2O_3 at 500°

30 g of furanidine was passed over chromic oxide on alumina (22.5% Cr_2O_3) at 500° at the rate of 8 drops per minute. This yielded 11.5 g of condensate (3.7 g of which was water); 14.1 liters of gas were evolved. The condensate, separated from the water and desiccated above calcium chloride, was distilled in a Favorsky flask into a narrow dephlegmator 45 cm high. Distillation of 7.5 g of the desiccated condensate yielded:

28-32° Fraction: n_D^{20} 1.4185 (0.6 g); and 32-66° fraction; n_D^{20} 1.4074 (0.2 g).

The remainder did not have a constant boiling point, distilling in the 66-260° range. The higher-boiling residue totaled 2.8 g.

Fraction 1 (b.p. of 28-32°) was furan (positive reaction for furan with pine chips wetted with concentrated hydrochloric acid); the refractive index of the resulting furan was somewhat lower than that of pure furan (n_D^{20} 1.4238), owing to minute quantities of furanidine that were hard to eliminate by distillation.

The gaseous reaction products were analyzed for O_2, CO, CO_2, unsaturated hydrocarbons (aggregate), butadiene, and hydrogen. The results of this gas analysis are given in Table 4.

TABLE 4

Composition of the Gas Evolved when Furanidine was Passed Over Cr_2O_3/Al_2O_3 at 500°

Quantity of gas evolved (NTP), liters	Per cent composition of the gas					
	O_2	CO	CO_2	Unsaturated hydrocarbons		H_2
				C_nH_{2n}	C_nH_{2n-2}	
14.1	0.4	0.25	11.0	23.0	6.0	59.0

The gas analysis data indicate that when the furanidine was passed over the chromic oxide on alumina, it was decomposed to propylene (C_nH_{2n}) [7], dehydrated to butadiene (C_nH_{2n-2}), and dehydrogenated, yielding furan and, probably, larger amounts of dihydrofuran, which then yielded the high-boiling polymers.

The butadiene was determined by the Korotkov method [11]; the propylene was determined by preparing 1,2-dibromopropane (11.2 g):

B.p. 139.5-140.5° (750 mm); n_D^{20} 1.5248; d_4^{20} 1.9329.

SUMMARY

The following conclusions may be drawn from the data secured in the conversion of furanidine into heterocyclic compounds containing nitrogen or sulfur by passing it over chromic oxide on alumina.

1. The optimum temperatures for converting furanidine into pyrrolidine or thiophane are below the optimum temperatures for similar transformations with alumina alone.

2. The yields of pyrrolidine and thiophane secured with chromic oxide on alumina at optimum temperature are considerably lower than those secured with alumina.

3. The conversion of furanidine into pyrrolidine at 350-500° with chromic oxide on alumina is accompanied by the dehydrogenation of the pyrrolidine into pyrrole, which reaches a maximum at 400°.

4. It has been established for the first time that the conversion of furanidine into pyrrolidine at 400-500° with chromic oxide on alumina also involves the formation of carbazole, its maximum yield occurring at 500°.

5. The probable reactions involved in the formation of carbazole from the pyrrole resulting from the dehydrogenation of pyrrolidine, on the one hand, and of butadiene or furan, resulting from the furanidine, on the other, are suggested and discussed.

6. It has been shown, for the first time, that furanidine can be dehydrogenated catalytically to furan at 500° in the presence of chromic oxide on alumina.

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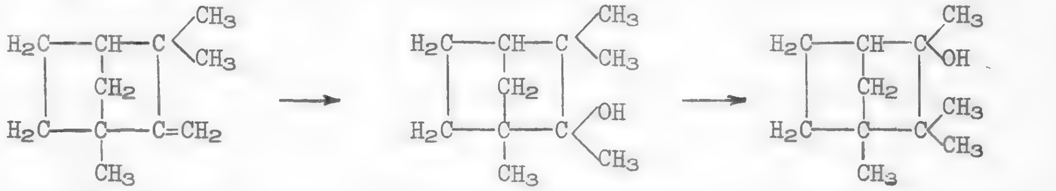
CAMPHENE REARRANGEMENTS AND THEIR OPTICAL CONSEQUENCES

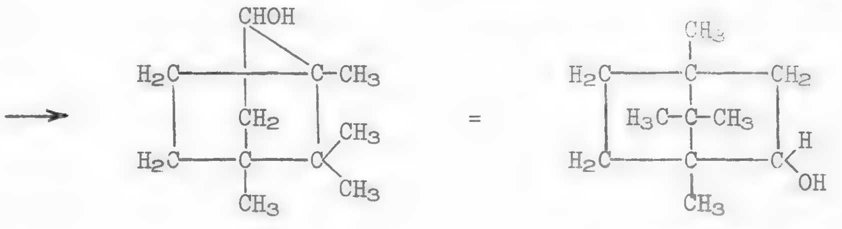
II. CHANGE IN OPTICAL ACTIVITY IN THE TRANSITION FROM TERT-PROPYLBORNEOL TO 4-PROPYLISOBORNEOL

A. I. Shavrygin

In contrast to the transition from optically active camphor to isoborneol, which always involves racemization when carried out in a Bertram-Wahlbaum reaction, the two 4-substituted isoborneols – 4-methylisoborneol and 4-propylisoborneol – prepared in our laboratory from the respective optically active α-substituted camphenes proved to be optically active [1]. This phenomenon was one of the basic points of departure for our subsequent research on the problem of racemization and optical reversal in the camphene rearrangement, which Bredt was the first to point out [2]. What is at issue here is that the formation of these optically active 4-substituted isoborneols from the respective optically active α-substituted camphenes occurs via a Class II camphene rearrangement, i.e., a double reversal of the sign of the rotatory power, as the result of reaction with glacial acetic acid to which sulfuric acid has been added. We generalized this and represented it by the following equations, using as our example the methyl-substituted homologs of camphene and isoborneol, [3].



(+) α-Methylcamphene [(+) α-Methylcamphene hydrate] [(-) β-Methylcamphene hydrate].



(+) 4-Methylisoborneol.

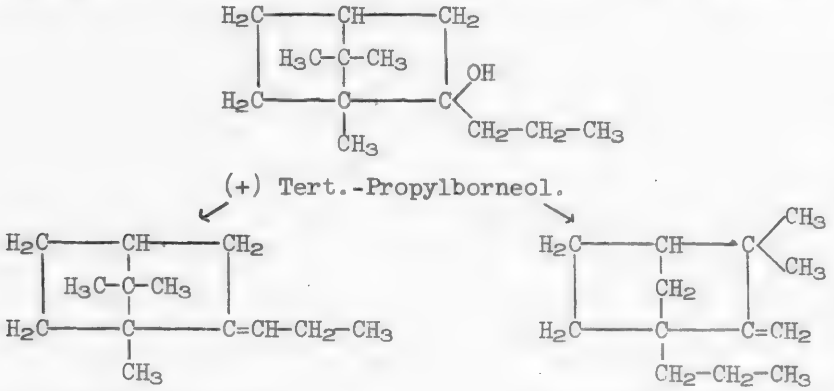
Obviously, a similar diagram could be used to represent the series of transformations from α-propylcamphene to 4-propylisoborneol, i.e., starting with dextrorotatory α-propylcamphene, we should secure dextrorotatory 4-propylisoborneol; this has been confirmed experimentally.

It should be noted, however, that the transformation of the optically active tert-propylborneol into the optically active 4-propylisoborneol is much more complicated than the transition from tert.-methylfenchyl alcohol to 4-methylisoborneol. Indeed, when tert.-propylborneol is dehydrated, we not only get the corresponding α-substituted camphene, as is the case in the dehydration of tert.-methylfenchyl alcohol, but also a mixture of two hydrocarbons – α-propylcamphene and propylidenecamphane, the latter being the principal dehydration product. This is borne out by the fact that the hydrocarbon mixture secured from the levorotatory tert.-propylborneol possesses the same levorotation, whereas the α-propylcamphene formed from the same alcohol via a Class I camphene rearrangement (a Wagner rearrangement) ought to be dextrorotatory according to the rule we have established experimentally. In fact, it has been shown in numerous instances [4] that dehydration of substituted tertiary bornyl alcohols takes place without changing the sign of rotation of the original alcohol, provided the dehydration does not involve isomerization. Whenever the dehydration is accompanied by a Wagner camphene rearrangement, the sign of rotation is reversed.

We were interested in checking whether these rules, viz.: a double change of the sign of rotation during a Class II camphene rearrangement and a reversal of the sign of rotation or its retention in the dehydration of tertiary bornyl alcohols, applied to the propyl-substituted homologs of the camphor group. From the logical point of view, all that we needed to settle the problem was to use levorotatory camphor instead of dextrorotatory camphor as our initial material. We could then make the *a priori* assumption that the change in the optical activity entailed by the conversion of tert-propylborneol into a secondary alcohol, 4-propylisoborneol, ought to be the opposite of what we had observed in our previous investigations.

Our experimental data confirmed this supposition. The tert.-propylbornyl alcohol prepared from levorotatory camphor turned out to be dextrorotatory, and its dehydration yielded, as we had expected, a hydrocarbon mixture of propylidene camphane and α-propylcamphene, which was likewise dextrorotatory. But when we reacted this hydrocarbon mixture with glacial acetic acid in the presence of sulfuric acid, after saponifying the corresponding ester, we ended up with a secondary alcohol, 4-propylisoborneol, that was levorotatory.

These experimental data on optical relationships definitely indicate that the dehydration of dextrorotatory tert.-propylborneol, like that of the levorotatory form, takes place in two ways. The first – the major pattern – results in the formation of propylidenecamphane, the sign of rotation remaining unchanged, and thus does not entail any isomerization of the bicyclic system of the tertiary alcohol. The second pattern results in the formation of α-propylcamphene, with the opposite sign of rotation, and hence entails a Wagner camphene rearrangement, i.e., a thoroughgoing isomerization of the carbon skeleton of the original tertiary alcohol:

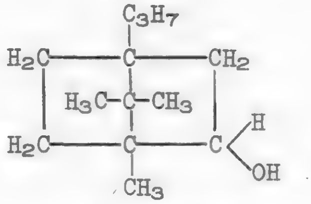


(+) Tert.-Propylborneol.

(+) Propylidenecamphane.

[(-)α-Propylcamphene].

The formation of α-propylcamphene as a constituent of the hydrocarbon mixture had been demonstrated experimentally in our previous investigations. As for the levorotation of the α-propylcamphene, this is borne out by the fact that the 4-propylisoborneol formed from it as a result of a series of transformations constituting a camphene rearrangement of the second order likewise was levorotatory, as indicated above:

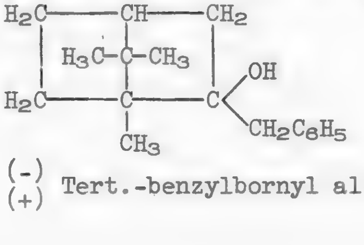


(-) 4-Propylisoborneol.

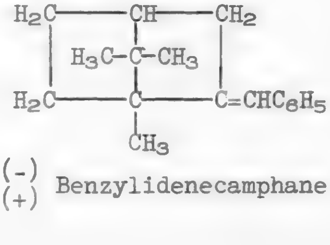
It may therefore be considered an established fact that the levorotatory 4-propylisoborneol is produced from the levorotatory α-propylcamphene, while the dextrorotatory 4-propylisoborneol is produced from the dextrorotatory α-propylcamphene. These results justify our concluding that here we have the same pattern of a change of optical activity that we observed in the transition from the dextrorotatory α-methylcamphene to the dextrorotatory 4-methylisoborneol, i.e., here too, a Class II camphene rearrangement entails a double change in the sign of rotation.

The second constituent of the hydrocarbon mixture formed by dehydrating tert.-propylborneol, propylidenecamphane, is also converted into 4-propylisoborneol by a reaction with glacial acetic acid and sulfuric acid; but in this process it is first isomerized to α-propylcamphene. The direct conversion of propylidenecamphane into an ester of 4-propylisoborneol without passing through the stage in which α-propylcamphene is formed is inconceivable. This is borne out by the experimental data secured in our laboratory [5], namely: numerous attempts to hydrate benzylidenecamphane with a view to securing the respective homologs of isoborneol and camphor via a Class II camphene rearrangement all met with failure.

It should be noted at this point that these negative results are also a splendid illustration of the rule we have established, namely, that the dehydration of substituted tertiary bornyl alcohols that does not involve a Wagner camphene rearrangement does not cause a change in the sign of rotation. In this connection, the transition from tert.-benzylbornyl alcohol to benzylidenecamphane is particularly interesting, since in this case the benzylidenecamphane is practically the only dehydration product, as we had noted earlier, besides being secured in crystalline form. In our previous investigations we had noted [4] that this transition actually causes no change in the sign of rotation. Levorotatory tert.-benzylborneol with $[\alpha]_D^{19}$ -23.12° yielded levorotatory benzylidenecamphane with $[\alpha]_D^{17}$ -67.97°. Here is further confirmation of the correctness of the rule. Dextrorotatory tert-benzylbornyl alcohol with $[\alpha]_D^{24}$ +22.96° was prepared from levorotatory camphor. Dehydrating it yielded benzylidenecamphane, which was likewise dextrorotatory, as was to be expected, with $[\alpha]_D^{22}$ + 68.54° The foregoing may be represented graphically as follows:



(-)
(+) Tert.-benzylbornyl alcohol.



(-)
(+) Benzylidenecamphane.

It has thus been twice established experimentally that in this instance the optical relationships are in full conformity with the mechanism involved in the dehydration of tert.-benzylbornyl alcohol. Inasmuch as no formation of the respective α-substituted camphene, with a farreaching change in the tertiary alcohol's bicyclic system, has ever been found to occur up to the present time, it is quite evident that no further transformations along the lines of a Class II camphene rearrangement could occur here.

EXPERIMENTAL

The initial material for the present research was levorotatory camphor, produced by oxidizing levorotatory borneol, which in turn had been isolated from pine oil. In the preparation of levorotatory camphor we followed in the main the procedure outlined by Golubev [6], who was the first to secure levorotatory camphor from pine oil and correctly evaluated the method he proposed. The intermediate products, especially the borneol, were carefully purified. The borneol had a m.p. of 205-206° after having been distilled with steam and recrystallized from petroleum ether.

Rotation in alcoholic solution: 1.2046 g; P 9.07%; d_4^{22} 0.8344; α -2.75° ($\underline{l}$ 1 dm); $[\alpha]_D$ -36.33°.

The borneol was oxidized to camphor in batches of 100 grams with nitric acid, sp. gr. 1.38-1.4. The reaction was carried out as follows in a round-bottomed flask with an outlet tube. Twice the weight of nitric acid was added to the borneol in a single batch. After some time had elapsed, a violent reaction set in, with the evolution of considerable heat. Then the reaction mixture was allowed to stand for some 4-5 hours at room temperature, being shaken up at intervals. The contents of the flask were then poured into a large volume of water. The camphor precipitated at once; it was suction filtered out and then twice distilled with steam in the presence of an alkali solution. The camphor was freed of water by dissolving it in ether, desiccating the ether solution with calcium chloride, driving off the ether, and desiccating the camphor in a desiccator. The camphor thus prepared had a yellowish tinge, a m.p. of 178-178.5°, the characteristic pleasant odor, and high optical activity.

Rotation in alcoholic solution: 1.2142 g; P 8.89%; d_4^{22} 0.8316; α -3.05° ($\underline{l}$ 1 dm); $[\alpha]_D$ 41.24°.

The camphor was rendered colorless by converting it via the semicarbazone; its melting point remained the same, but its rotatory power in alcoholic solution increased somewhat.

1.2026 g; P 8.86%; d_4^{25} 0.8320; α -3.10° ($\underline{l}$ 1 dm); $[\alpha]_D$ -42.06°.

Tert-allylbornyl alcohol. This was prepared in the usual manner, i.e., by reacting camphor with magnesium and allyl bromide. Eight tests were made, 20 g of camphor being used in each test. All the tests were successful. The alcohol was purified by fractional distillation; b.p. 124-126° at 22 mm.

Rotation in alcoholic solution: 1.2312 g; P 9.17%; d_4^{25} 0.8340; α + 1.15° ($\underline{l}$ 1 dm); $[\alpha]_D$ +15.04°.

Tert.-propylbornyl alcohol. This was produced by hydrogenating 167 g of allylbornyl alcohol with a nickel catalyst. The reaction was carried out at room temperature in a 1:2 alcoholic solution, with vigorous mechanical stirring of the reaction mixture; the yield was good. After appropriate further processing, the tert.-propylborneol was fractionated. Part of the alcohol distilled at 247-249° (744 mm); it proved to be a liquid that solidified completely upon cooling. The bulk of the residue distilled at the same pressure at 249-250° and solidified at room temperature; the m.p. of this portion of the product was 30-31.5° (in a test tube), i.e., the same as that of the levorotatory tert.-propylborneol secured previously.

Rotation in alcoholic solution: 1.2248 g; P 9.25%; d_4^{24} 0.8359; α + 0.95° (l 1 dm); $[\alpha]_D$ + 12.29.

3.560 mg substance: 10.355 mg CO_2; 3.955 mg H_2O. Found %: C 79.33; H 12.43. $C_{13}H_{24}O$. Computed %: C 79.51; H 12.33.

The dextrorotatory tert.-propylborneol is a stable compound that distils at ordinary pressure without splitting out water and has a pleasant pine odor.

Dehydration of tert.-propylborneol. In our previous paper we proved that the reaction of tert.-propylborneol with glacial acetic acid and sulfuric acid is chiefly a dehydration of the alcohol, resulting in a hydrocarbon mixture of propylidenecamphane and α-propylcamphene. The α-propylcamphene also yields a small amount of the respective acetate, saponification of which produces a secondary alcohol: 4-propylisoborneol. We repeated these experiments, and we shall cite the results of one of them. 81 g of tert.-propylborneol was heated over a water bath to 55-60° for 25 hours with three times it weight of glacial acetic acid in the presence of 8 g of 50% sulfuric acid. After the subsequent customary processing, the reaction product was fractionated in vacuum. Most of it distilled at 98-99° at 20 mm.

d_4^{20} 0.8725; n_D^{20} 1.4780; MR_D 57.79; computed 57.37.

The difference between the observed and computed molar refraction is evidence of the semicyclic nature of the double bond in the hydrocarbon.

Rotation without a solvent. (l 1 dm); α +29.92°; $[\alpha]_D^{24}$+34.29°.

3.165 mg substance: 10.180 mg CO_2; 3.530 mg H_2O. 3.310 mg substance: 10.650 mg CO_2; 3.740 mg H_2O. Found %: C 87.72, 87.75; H 12.48, 12.64. $C_{13}H_{22}$. Computed %: C 87.55; H 12.45.

All of the properties of the distilled product indicate that it is a mixture of propylidenecamphane and α-propylcamphene, the only difference being that now the sign of rotation is reversed, as was to be expected.

4-Propylborneol. After the bulk of the hydrocarbon mixture had been distilled off, there remained a residue (10.5 g) in the distilling flask that consisted of a hydrocarbon and the 4-propylborneol acetate that had been formed. This residue was saponified with an aqueous-alcoholic alkali over a boiling water bath for 4-5 hours, without separating the acetate. The usual processing and vacuum distillation of the hydrocarbon yielded 3.1 g of 4-propylisoborneol. After being squeezed out on a porous plate, the coarsely crystalline 4-propylborneol exhibited the expected levorotation, $[\alpha]_D^{23}$ -9.96°.

Rotation without a solvent: 1.2016 g; P 9.64%; d_4^{23} 0.8333; α -0.8° (l 1 dm); $[\alpha]_D$ -9.96°.

3.155 mg substance: 9.165 mg CO_2; 3.540 mg H_2O. Found %: C 79.22; H 12 56. $C_{13}H_{24}O$. Computed %: C 79.51; H 12.23.

The levorotatory 4-propylisoborneol, like its dextrorotatory stereoisomer, had a m.p. of 57-58°, and a mixture of the two fused at the same temperature. As we had found in our previous investigations, repeated hydrations of the hydrocarbon mixture resulted in the partial formation of 4-propylisoborneol; the properties of the distilled hydrocarbon mixture that had not entered into the reaction were unchanged, except for the rotation, which grew progressively smaller.

Tert. benzylbornyl alcohol was prepared by reacting an ethereal solution of the levorotatory camphor with benzylmagnesium chloride. After the usual subsequent processing and the elimination of the unreacted camphor and of the dibenzyl that was a reaction by-product, the tertiary alcohol distilled at 162-163° (at 6 mm).

Rotation in alcoholic solution: 1.0246 g; P 7.85%; d_4^{24} 0.8316; α + 1.50° ($\underline{l}$ 1 dm); $[\alpha]_D$ + 22.96°.

Benzylidenecamphane was prepared by heating the dextrorotatory tert.-benzylbornyl alcohol with twice its weight of potassium bisulfite to 150-160° for 3 hours over an oil bath. After the usual processing, the hydrocarbon distilled at 150-151° in a 6-mm vacuum.

Rotation in alcoholic solution: 1.0044 g; P 5.92%; d_4^{20} 0.8621; α +3.25° ($\underline{l}$ 1 dm); $[\alpha]_D$ +66.46°.

The benzylidenecamphane had a rotatory power of $[\alpha]_D^{22}$ + 68.54 in alcoholic solution after it had been recrystallized from an excess of alcohol.

0.5540 g; P 3.28%; d_4^{22} 0.8266; α +1.85° ($\underline{l}$ 1 dm); $[\alpha]_D$ +68.54°.

The levorotatory benzylidenecamphane had a rotatory power of $[\alpha]_D^{17}$ -67.97° in the same solvent.

The melting point of the dextrorotatory benzylidenecamphane was 25-25.5° (in a test tube), i.e., the same as its levorotatory stereoisomer. A mixture of the two hydrocarbons fused at the same temperature.

d_4^{30} 0.9750; n_D^{30} 1.5630; MR_D 75.34; computed 72.24.

2.760 mg substance: 9.115 mg CO_2; 2.400 mg H_2O. 2.995 mg substance: 9.89 mg CO_2; 2.640 mg H_2O. Found %: C 90.07, 90.06. H 9.73, 9.86. $C_{17}H_{22}$. Computed %: C 90.19; H 9.81.

As we see, the optical exaltation of the dextrorotatory benzylidenecamphane is rather high, 3.10. According to Nametkin and Strugatsky [5], the optical exaltation of levorotatory benzylidenecamphane is almost the same, 3.07. The reason for this discrepancy is evidently (as these authors point out) the peculiar structure of benzylidenecamphane, namely, its possessing a semicyclic double bond conjugated with a double bond in the benzene ring. Thus, all the properties of these two hydrocarbons are the same, within the limits of experimental error, except for the fact that they exhibit opposite rotation.

	Melting point	d_4^{30}	n_D^{30}	MR_D observed	$[\alpha]_D$
$\underline{l}$-Benzylidenecamphane*	25°	0.9753	1.56280	75.31	-67.97°
$\underline{d}$-Benzylidenecamphane	25-25.5	0.9750	1.5630	75.34	+68.54

As we have stated above, transitions from dextro- and levorotatory tert.-benzylbornyl alcohols to the respective dextro- and levorotatory benzylidenecamphanes (with no change in the sign of rotation) are of special importance in a study of the mechanism involved in the dehydration of substituted tert.-bornyl alcohols as well as in ascertaining the feasibility of Class II camphene rearrangements.

Our research is being continued.

SUMMARY

The optical consequence of camphene rearrangements that we have established previously, to wit: the double change in the sign of rotation during a Class II camphene rearrangement; the reversal of the sign of rotation during a Class I

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*The properties of $\underline{l}$-benzylidenecamphane have been taken from Nametkin and Strugatsky [5] with the exception of its optical activity.

camphene rearrangement; and, lastly, the retention of the sign of rotation whenever the dehydration of the substituted tertiary bornyl alcohols does not involve isomerization, have received further experimental confirmation in the present report.

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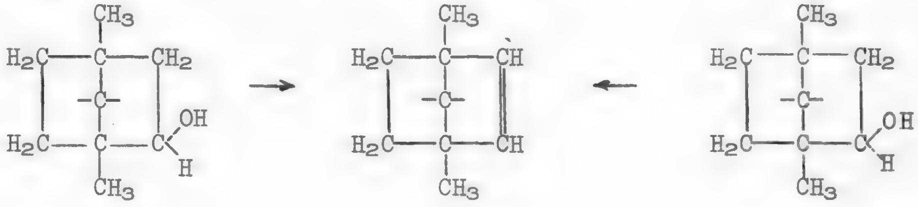
THE ISOMERIZATION OF ISOBORNEOL AND 4-METHYLISOBORNEOL WHEN DEHYDRATED BY THE XANTHOGENIC METHOD

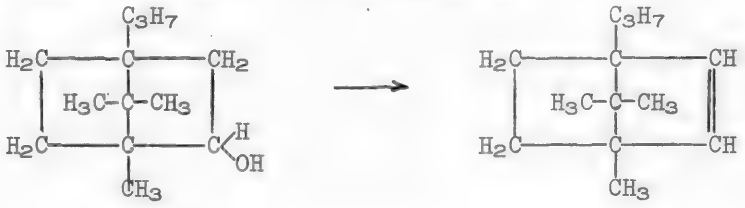
A. I. Shavrygin

In determining whether isoborneol is a secondary or tertiary alcohol, the application to isoborneol and its homologs of Chugaev's xanthogenic reaction, which as a rule does not cause any isomerization of the carbon skeleton of the original alcohol, is doubtless of primary importance. In support of the foregoing statement we can cite some experimental data that we secured in our preceding investigations. We found [1] that the xanthogenic dehydration of two very close homologs of isoborneol and borneol, 4-methylisoborneol (I) and 4-methylborneol (II), respectively, yielded the same unsaturated hydrocarbon, 4-methylbornylene (III).



(I) (III) (II)

The formation of the normal dehydration product, 4-methylbornylene, in this case indicates: 1) that the two alcohols have the same structure, and 2) that 4-methylisoborneol is a secondary alcohol, the geometrical isomer of 4-methylborneol. Dehydration of 4-propylisoborneol (IV) by the same xanthogenic method likewise proved to take place normally, as we have established [2], resulting in the normal reaction product, 4-propylbornylene (V).



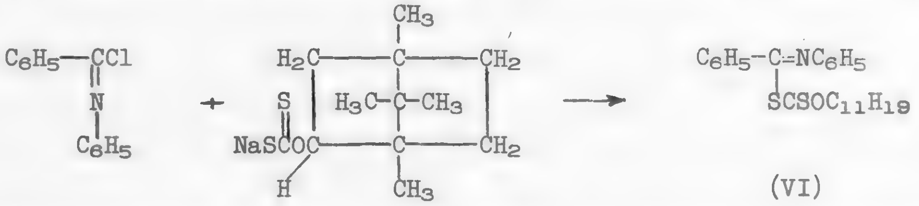
(IV) (V)

Here again, the formation of 4-propylbornylene indicates that 4-propylisoborneol is a secondary alcohol.

Less satisfactory results were achieved in our study of the dehydration of isoborneol by the Chugaev method [3]. Although the same bornylene was formed as is produced from borneol under similar conditions, about the same quantity of camphene was formed. The parallel formation of bornylene and camphene may be due to the fact that the dehydration of isoborneol, in contrast to that of its 4-substituted homologs, is accompanied by a partial, far-reaching isomerization of the carbon skeleton of some of the isoborneol to a camphene system. This isomerization is evidently due to the lesser stability of the isobornyl xanthate. When a rather high temperature, about 200° or somewhat higher, is maintained during the decomposition of the latter, we get camphene as well as bornylene.

The cited experimental data thus indicate that isoborneol and its 4-substituted homologs, 4-methylisoborneol and 4-propylisoborneol, are all secondary alcohols, geometrical isomers of the respective borneols. This conclusion is correct only provided dehydration by the xanthogenic method does not entail isomerization of the isoborneol to borneol, or that of its 4-substituted homologs to the respective 4-substituted homologs of borneol.

In the present paper we have made an effort to resolve this problem, using the synthesis and comparison of some derivatives that are directly linked to bornyl- and isobornylxanthic acids and to 4-methylbornyl- and 4-methylisobornylxanthic acid. We must first mention our synthesis of imido xanthides from 4-methylborneol and 4-methylisoborneol, i.e., two new representatives of the terpenes of this interesting class of colored organic compounds first discovered by Chugaev [4]. Inasmuch as the imido xanthides are formed by reacting aromatic imide chlorides with sodium or potassium xanthates, we started with the sodium salt of 4-methylisobornylxanthic acid and diphenylimide chloride and secured, in Chugaev's terminology, 1,2-diphenyl-3,4-methylisobornylimido xanthide, as follows:

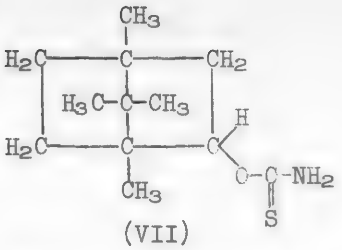


(VI)

1,2-Diphenyl-3,4-methylisobornylimido xanthide is a bright-red crystalline substance with a m.p. of 112-113°. Starting with the sodium salt of 4-methylbornylxanthic acid, we prepared 1,2-diphenyl-3,4-methylbornylimido xanthide by a similar reaction; it also was a bright-red crystalline substance, with a m.p. of 116-117°.

Our efforts to synthesize an imido xanthide by starting out with the sodium salt of isobornylxanthic acid met with failure. The colored solution formed initially was nearly completely decolorized when the solvent (benzene) was driven off with steam, which is in full conformity with Chugaev's assertions [5]. As he justly points out, this is due to the extremely low stability of isobornylimidoxanthide. But this same circumstance doubtless indicates that dehydration of isoborneol by the xanthogenic method does not involve its isomerization to borneol. If this sort of isomerization did take place, we should have secured bornylimido xanthide in the foregoing experiment.

Besides the imido xanthides, we synthesized two xanthogenamides. Starting out with ethyl isobornyl xanthate, we synthesized isobornylxanthogenamide, with a m.p. of 130-131°; according to Chugaev [6], racemic bornylxanthogenamide has a m.p. of 134.5-135.5°. From ethyl 4-methylisobornyl xanthate we synthesized 4-methylisobornylxanthogenamide (VII), with a m.p. of 121-122°; according to L. Ya. Bryusova [7], 4-methylbornylxanthogenamide has a m.p. of 126-127°. It should be noted that the imido xanthide synthesized from 4-methylisoborneol and the xanthogenamides synthesized from 4-methylisoborneol and isoborneol have melting points that lie below those of the corresponding compounds synthesized from



(VII)

4-methylborneol and borneol. Similarly, the ethyl ester of carbanilic acid and the acid phthalic ester of 4-methylisoborneol have lower melting points than the respective derivatives of 4-methylborneol [8].

EXPERIMENTAL

(In association with V. L. Kostomarovaya)

1,2-Diphenyl-3,4-methylisobornylimido xanthide (VI). The initial compounds we used to synthesize this imido xanthide were 4-methylisoborneol, prepared from α-methylcamphene [8], and diphenylimide chloride, prepared by the Wallach method [9]. The usual reaction was employed to secure the sodium salt of 4-methylisobornylxanthic acid from 4-methylisoborneol. 5 g of diphenyl imido chloride and 7.8 g (an excess) of the sodium salt of 4-methylisobornylxanthic acid dissolved in 100 ml of anhydrous benzene were heated together over a water bath for 5 hours. The solution turned dark red. When the reaction was over, the benzene was driven off with steam, and the residue – a dark-red mass – was extracted with ether. The ether solution was washed with water, and then about half its volume of alcohol was added. When the solvent was evaporated slowly, the red crystals of the imidoxanthide settled out. They were filtered out and treated 2 or 3 more times with an ether alcohol mixture; this yielded pure 1,2-diphenyl-3,4-methylisobornylimido xanthide as bright red crystals with a m.p. of 112-113°.

0.4026 g substance: 9.74 ml 0.1 N HCl. Found %: N 3.39.
$C_{25}H_{29}ONS_2$. Computed %: N 3.31.

1,2-Diphenyl-3,4-methylbornylimido xanthide. This imido xanthide was synthesized by reacting 6 g of diphenylimido chloride with 8 g of the sodium salt of 4-methylbornylxanthic acid. The reaction was carried out as described above. Treatment with an ether-alcohol mixture 2 or 3 times yielded pure 1,2-diphenyl-3,4-methylbornylimido xanthide – bright-red crystals with a m.p. of 116-117°.

0.3664 g substance: 8.38 ml 0.1 N HCl. Found %: N 3.20.
$C_{25}H_{29}ONS_2$. Computed %: N 3.31.

4-Methylisobornylxanthogenamide (VII). This xanthogenamide was synthesized from the methyl ester of 4-methylisobornylxanthic acid and about 10% alcoholic ammonia, used in excess. The reaction mixture was allowed to stand for 7 days at room temperature, and then it was poured into a large quantity of water. The resultant precipitate – colorless minute needles – was recrystallized from a mixture of two parts of petroleum ether and three parts of benzene. The 4-methylisobornylxanthogenamide had a m.p. of 121-122° after having been dried in a desiccator.

0.2334 g substance: 10.70 ml 0.1 N HCl. Found %: N 6.42.
$C_{12}H_{21}ONS$. Computed %: N 6.16.

Isobornylxanthogenamide. To synthesize this xanthogenamide we prepared isoborneol with a m.p. of 211-212° from camphene, and from this isoborneol, via its xanthate, we prepared the methyl ester of isobornylxanthic acid. The latter was a yellow oil that did not solidify after having been chilled for a long time [10]. We then prepared the amide in the usual fashion from the xanthate and an excess of about 10% alcoholic ammonia. Isobornylxanthogenamide was recovered as prismatic crystals from a hot solution in a 2:3 mixture of petroleum ether and benzene; its m.p. was 130-131° after drying in a desiccator.

0.2502 g substance: 12.15 ml 0.1 N HCl. Found %: N 6.79.
$C_{11}H_{19}ONS$. Computed %: N 6.57.

Our research is continuing.

SUMMARY

The described experimental data on the formation of imido xanthides and xanthogenamides contradict the assertion that xanthogenic dehydration involves the isomerization of isoborneol to borneol and of 4-substituted homologs of isoborneol to the corresponding 4-substituted homologs of borneol. On the contrary, the data cited support the nearly universally held view of the stereochemical nature of the relationship between isoborneol and isoborneol and borneol as secondary alcohols that are geometrical isomers.

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SYNTHESIS OF SUBSTANCES POSSESSING ANTITHYREOIDIN ACTIVITY

III. S-METHYL-6 DERIVATIVES OF THIOURACIL

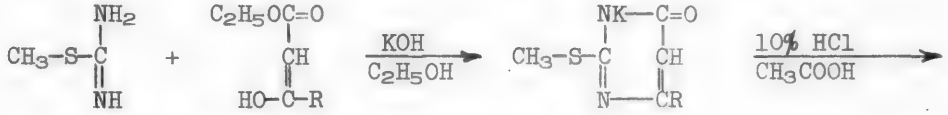
I. B. Simon and I. I. Kovtunovskaya

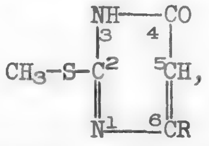
In our previous reports [1,2] we have shown that introducing a methyl group at the 6 position into 2-thiouracil increases the latter's antithyreoidin activity somewhat. 6-Methylthiouracil causes a greater decrease in the colloidal substance of the thyroid gland than 2-thiouracil does, for example; moreover, it is less toxic, not affecting the number of red or white corpuscles over a long period of time. It was also shown [2] that other 6-derivatives of thiouracil, such as 6-ethyl-, 6-n-propyl-, 6-benzyl-, and 6-n-butylthiouracil, possess no significant clinical advantages over 6-methylthiouracil, notwithstanding the fact that some American authors [3] claim they are from 3 to 10 times as effective as 2-thiouracil (in experiments on rats). In our search for preparations of higher antithyreoidin activity, beginning in 1945, we have shown that it is advisable to combine two antithyreoidin principles of different types. Thus, by combining sulfanilamide in the N^4 position with thiourea or with aminothiazole, we can detach each of the constituents within the organism separately, which promotes an increase in the antithyreoidin action of the preparation as a whole. Such compounds as N-parabenzenesulfonamidothiocarbamide, 2-(parabenzenesulfonamidoamino)-thiazole, and 2-(parabenzenesulfonamidoamino)-4-methylthiazole proved to be more active in tests on rats [2,4] than thiourea, 2-thiouracil, or 6-methylthiouracil.

In contradiction to the American investigations [3], we showed [2] that the methyl, ethyl, and methylene derivatives of isothiourea exhibit much greater activity in the form of their hydriodides than thiourea itself. We therefore thought it would be interesting to make a study of the effect of a methyl group attached to the sulfur upon increasing the antithyreoidin activity of several 6-derivatives of thiouracil (6-methyl-, 6-ethyl-, 6-n-propyl-, 6-n-butyl-, 6-phenyl-, and 6-benzylthiouracil).

We synthesized the S-methyl-6-derivatives of thiouracil in two ways:

1) by condensing S-methylisothiourea with the respective esters of β-keto acids as follows:





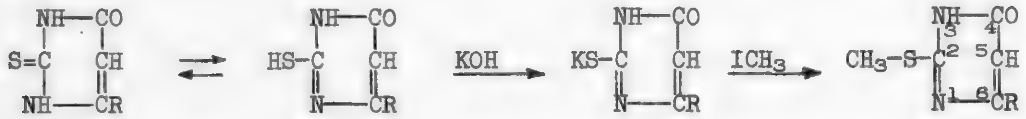
where R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_6H_5, $CH_2C_6H_5$.

S-6-Dimethyl-, S-methyl-6-benzyl-, S-methyl-6-phenyl-, and S-methyl-6-n-butylthiouracil were synthesized by condensing molar quantities of S-methylisothiourea with an ester of the β-keto acid in the presence of an excess (2 mols) of potassium hydroxide. The mixture was allowed to stand for 48 hours, after which it was filtered and the filtrate acidulated with acetic acid.

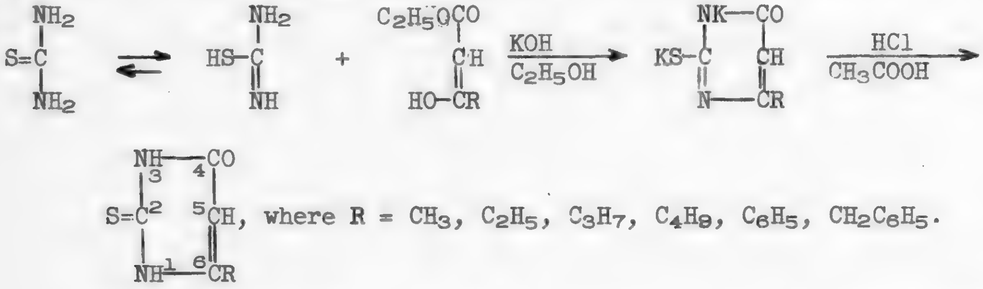
S-Methyl-6-ethyl- and S-methyl-6-n-propylthiouracil were synthesized by heating S-methylisothiourea hydriodide for an hour over a water bath with an ester of the β-keto acid in an alcoholic solution of sodium ethylate.

We prepared the hydriodide of S-methylisothiourea by the method described by us previously [1].

2) By methylating the 6-derivatives of thiouracil with an excess of methyl iodide:



The 6-Derivatives of thiouracil were prepared by condensing thiourea with the respective esters of the β-keto acids as follows:



where R = CH_3, C_2H_5, C_3H_7, C_4H_9, C_6H_5, $CH_2C_6H_5$.

Condensation of the esters of the β-keto acids with thiourea to yield the 6-derivatives of 2-thiouracil was effected by a method we had developed earlier to synthesize 6-methyl-2-thiouracil. This method is based upon heating of the ester (1.1 mole with thiourea (1 mole) in the presence of an alcoholic solution of potassium hydroxide (0.8 mole) for half an hour over a water bath. Then the alcohol is driven off, the dry residue is dissolved in water, and the solution is acidulated with 10% hydrochloric or acetic acid. The regenerated alcohol is reused.

The 6-derivatives of thiouracil were methylated by reacting a molar quantity of the 6-derivatives of thiouracil for 20-30 hours with an excess of methyl iodide in the presence of an aqueous solution of potassium hydroxide (2 mols). Acidulation with acetic acid yielded the respective methyl derivative.

EXPERIMENTAL

A. Synthesis of the Intermediate Products

Ethylphenylacetylacetate was synthisized by a modified Sonn and Litten method [5]. 2.4 g of metallic sodium was added to 14 g of acetoacetic ester dissolved in 140 ml of absolute ether. After having been stirred for 3 hours, the reaction mixture was set aside until the next day, when it was heated for 4 hours over a water bath, with constant stirring, until all the metallic sodium had dissolved. 8.5 g of the acid chloride of phenylacetic acid and 30 ml of absolute ether were then added drop by drop to the reaction mass, which was stirred and chilled with ice water. The resultant yellow precipitate, which was a mixture of the sodium derivative of ethylphenylacetylacetoacetate and sodium chloride, was filtered out, washed with ether, and dissolved in water that had been acidulated with acetic acid. The oil that separated out was extracted with ether. The ether extract of the product was washed with water and then agitated for an hour with 200 ml of 1% aqueous ammonia to split out the acetyl group. The aqueous ammoniacal solution was treated several times with ether. The ether extracts were washed with sodium bicarbonate and with water and then desiccated with sodium sulfate. The ether was driven off, and the residue – a thick oil – was twice distilled in vacuum. Ethylphenylacetylacetate was a transparent liquid with a b.p. of 153-155° at 9 mm. The yield was 3.5 g (31% of the theoretical).

Ethyl cyanacetate was prepared by the method described in Syntheses of Organic Preparations [Vol. I, p. 262 (1932)], as modified by us. The cyanacetic acid was esterified with 96% ethyl alcohol instead of the absolute alcohol called for in the published recipe; this has no effect upon the yield of the ethyl cyanacetate.

Ethyl butyrylacetate, with b.p. of 94-96° at 15 mm (40% yield) and ethyl valerylacetate, with a b.p. of 128-130° at 20 mm (42% yield) were prepared by the method described by Anderson and his coworkers [6] for the synthesis of ethyl propionylacetate.

6-Ethylthiouracil. 1.6 g of thiourea and 3.2 g of ethyl propionylacetate were added to 2 g of potassium hydroxide dissolved in 2 ml of water and 5 ml of alcohol. The mixture was heated for half an hour over a water bath in a flask fitted with a reflux condenser. Then the alcohol was driven off, and the residue dissolved in water and acidified with an acetic acid solution until precipitation was complete. The precipitate was recrystallized from alcohol. Yield: 1.7 g (50%); m.p. 227°.

6-Propylthiouracil. 1.7 g of ethyl butyrylacetate and 0.8 g of thiourea were added to 1 g of potassium hydroxide in 1 ml of water and 10 ml of ethyl alcohol. The product was isolated as set forth above. The precipitate was recrystallized from hot water. Yield: 0.9 g (50%). M.p. 217°.

6-Butylthiouracil. 4.0 g of ethyl valerylacetate and 1.8 g of thiourea were added to a solution of sodium ethylate, prepared with 0.6 g of metallic sodium and 10 ml of rectified alcohol. The product was isolated as described above for the preparation of 6-ethylthiouracil. The precipitate was recrystallized from aqueous alcohol. Yield: 1 g (53%). M.p. 206°.

6-Phenylthiouracil. 3.8 g of ethylbenzoylacetate and 1.5 g of thiourea were added to a solution of sodium ethylate, prepared with 0.5 g of metallic sodium and 25 ml of ethyl alcohol. The product was isolated as described above. The precipitate was recrystallized from aqueous alcohol. Yield: 0.9 g (30% of the theoretical). M.p. 263°.

6-Benzylthiouracil. 0.8 g of ethyl phenylacetylacetate and 0.29 g of thiourea were added to a solution of sodium ethylate, prepared with 0.09 g of metallic sodium and 10 ml of ethyl alcohol. The product was isolated as described above. The precipitate was recrystallized from ethyl alcohol. Yield: 0.3 g (39% of the theoretical). M.p. 221°.

3.70 mg substance: 0.43 ml N_2 (22°, 754 mm); 4.822 mg substance: 0.555 ml N_2 (22°, 754 mm). Found %: N 13.07, 12.95; $C_{11}H_{10}ON_2S$. Computed %: N 12.84.

B. Synthesis of the S-Methyl-6 Derivatives of Thiouracil

S-6-Dimethylthiouracil. 1) 8.7 g of S-methylisothiourea hydriodide and 5.2 g of freshly distilled acetoacetic ester were added to 2.2 g of potassium hydroxide dissolved in 1.5 ml of water. The mixture was allowed to stand for 6 hours, then was filtered, acidified with acetic acid until precipitation was complete. The precipitate was filtered out and recrystallized from hot water. Yield 2 g (32%). M.P.

224-225°. Wheeler gives the m.p. as 219° [7].

2) 2.8 g of 6-methylthiouracil was added to 2.2 g of potassium hydroxide dissolved in 1.5 ml of water, and after dissolution was complete, 8.4 g of methyl iodide was added. The mixture was allowed to stand overnight. The next day the solution was acidulated with acetic acid until precipitation was complete. The precipitate was recrystallized from hot water. Yield: 2 g (66%). M.p. 224-225°. A mixture of the substances prepared by Methods 1 and 2 fused at 224°.

S-Methyl-6-ethylthiouracil. 1) 6.5 g of S-methylisothiourea was added to 1.7 g of potassium hydroxide dissolved in 3 ml of water, and after dissolution was complete, 4.3 g of ethyl propionylacetate was added. The reaction product was isolated by the Method 1 used for the synthesis of S-6-dimethylthiouracil. The yield of the product was 1.4 g (28%) after recrystallization from alcohol; m.p. 153°.

5.411 mg substance: 0.7968 ml N_2 (24°, 750 mm). 4.808 mg substance: 0.7262 ml N_2 (24°, 750 mm). Found %: N 16.72, 16.69;
$C_7H_{10}ON_2S$. Computed %: N 16.47.

2) 0.5 g of 6-ethylthiouracil and 0.9 g of methyl iodide were added to 0.4 g of potassium hydroxide dissolved in 1 ml of water. The rest of the synthesis was the same as that used in Method 2 for the synthesis of S-6-dimethylthiouracil. The precipitate was recrystallized from hot water. Yield: 0.3 g (60%). M.p. 153°. A mixture of the substances prepared by Methods 1 and 2 fused at 153°.

3.816 mg substance: 0.555 ml N_2 (22°, 757 mm). 3.605 mg substance: 0.53 ml N_2 (24°, 757 mm). Found %: N 16.43, 16.50.
$C_7H_{10}ON_2S$. Computed %: N 16.47.

S-Methyl-6-propylthiouracil. 1) 2.7 g of S-methylisothiourea hydriodide and 2 g of ethyl butyrylacetate were added to 0.7 g of potassium hydroxide dissolved in 3 ml of water. The product was isolated as specified above. The precipitate was recrystallized from water. Yield: 0.5 g (21%). M.p. 154°.

2) 0.2 g of propylthiouracil and 0.3 g of methyl iodide were added to 0.1 g of potassium hydroxide dissolved in 0.5 ml of water. The product was isolated as specified in the experiment on the synthesis of S-6-dimethylthiouracil. The precipitate was recrystallized from dilute alcohol. Yield: 0.08 g (38% of the theoretical). M.p. 154-155°. A mixture of the substances prepared by Methods 1 and 2 fused at 155°.

5.012 mg substance: 0.675 ml N_2 (24°, 750 mm). 5.005 mg substance: 0.680 ml N_2 (22°, 750 mm). Found %: N 14.99, 15.20.
$C_8H_{12}ON_2S$. Computed %: N 15.21.

S-Methyl-6-butylthiouracil. 1) 2.1 g of S-methylisothiourea and 1.7 g of ethyl valerylacetate were added to 0.6 g of potassium hydroxide dissolved in 1 ml of water. The product was isolated as specified in the experiment on the synthesis of S-6-dimethylthiouracil (Method 1). The precipitate was recrystallized from aqueous alcohol. Yield: 0.4 g (21%). M.p. 127°.

3.814 mg substance: 0.488 ml N_2 (24°, 745 mm). 3.60 mg substance: 0.460 ml N_2 (24°, 755 mm). Found %: N 14.13, 13.74.
$C_8H_{14}ON_2S$. Computed %: N 14.14.

2) 0.18 g of butylthiouracil and 0.06 g of methyl iodide were added to 0.01 g of sodium hydroxide in 0.6 ml of alcohol. The reaction mixture was heated to 60° for 20 minutes. Then it was cooled and acidulated with acetic acid. Nothing was precipitated thereby. The solution was evaporated until nearly dry, and the residue was twice recrystallized from hot water. Yield 0.4 g (21%). M.p. 127°. A mixture of the substances prepared by Methods 1 and 2 fused at 126-127°.

S-Methyl-6-phenylthiouracil. 1) 4.3 g of S-methylisothiourea and 3.8 g of ethyl benzoylacetate were added to 1.1 g of potassium hydroxide dissolved in 2 ml of water. The product was isolated as indicated in the experiment on the synthesis of S-6-dimethylthiouracil (Method 1). The precipitate was twice recrystallized from alcohol. Yield: 1.2 g (29% of the theoretical). M.p. 241°.

3.806 mg substance: 0.455 ml N_2 (22°, 745 mm). 3.810 mg substance: 0.446 ml N_2 (24°, 747 mm). Found %: N 13.29, 12.96.
$C_{11}H_{10}ON_2S$. Computed %: N 12.84.

2) 0.5 g of methyl iodide and 0.4 g of phenylthiourea were added to 0.2 g of potassium hydroxide dissolved in 2 ml of water. The product was isolated as indicated in the experiment on the synthesis of S-6-dimethylthiouracil (Method 2). The precipitate was twice recrystallized from alcohol. Yield: 0.26 g (62% of the theoretical). M.p. 240°. A mixture of the substances synthesized by Methods 1 and 2 fused at 240°.

3.416 mg substance: 0.403 ml N_2 (22°, 755 mm). 3.410 mg substance: 0.108 ml N_2 (22°, 755 mm). Found %: N 13.29, 12.48.
$C_{11}H_{10}ON_2S$. Computed %: N 12.84.

S-Methyl-6-benzylthiouracil. 1) 2.1 g of S-methylisothiourea hydriodide and 2 g of ethyl phenylacetylacetate were added to 0.6 g of potassium hydroxide in 1 ml of water. The product was isolated as indicated in the experiment on the synthesis of S-6-dimethylthiouracil (Method 1). The precipitate was recrystallized from aqueous alcohol. Yield: 0.8 g (32% of the theoretical). M.p. 180°.

3.604 mg substance: 0.40 ml N_2 (22°, 746 mm). 4.82 mg substance: 0.545 ml N_2 (22°, 746 mm). Found %: N 12.35, 12.58.
$C_{12}H_{12}ON_2S$. Computed %: N 12.07.

2) 0.3 g of methyl iodide and 0.4 g of benzylthiouracil were added to 0.2 g of potassium hydroxide dissolved in 1 ml of water. The mixture was allowed to stand for 60 hours. The product was isolated as indicated in the experiment on the synthesis of S-6-dimethylthiouracil. The precipitate was recrystallized from dilute alcohol. Yield: 1.1 g (26% of the theoretical). M.p. 178°. A mixture of the preparations synthesized by Methods 1 and 2 had the m.p. of 180°.

SUMMARY

A number of the S-methyl-6 derivatives of thiouracil has been synthesized in two ways: a) by condensing the respective esters of β-keto acids with isothiourea; and b) by methylating the 6-derivatives of thiouracil with an excess of methyl iodide.

We have thus synthesized S-6-dimethylthiouracil, S-methyl-6-phenylthiouracil, S-methyl-6-ethylthiouracil, S-methyl-6-n-propylthiouracil, S-methyl-6-n-butylthiouracil, and S-methyl-6-benzylthiouracil. The latter four compounds have not been described in the literature.

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THE ACTION OF CHLOROSULFONIC ACID UPON 2-CYANACETYLCOUMARONE

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It is common knowledge that coumarone and many of its derivatives are readily polymerized by concentrated sulfuric acid, the composition of the polymers depending upon the concentration of the acid and the quantity used. When these polymers are heated with concentrated sulfuric acid, sulfonated products are apparently formed, though it has not been possible to isolate them as free sulfo acids or as salts, owing to the fact that they do not crystallize, [1].

When coumarone is reacted with chlorosulfonic acid in neutral solvents (such as ether), the acid adds a furan ring at its double bond. Treatment with water causes the chlorine to be replaced by a hydroxyl group, and the resulting sulfo acid of dihydroxycoumaran, $C_8H_6O(OH)SO_3H$, is salted out as its sodium salt by means of sodium chloride [2].

When chlorosulfonic acid is reacted with several coumarones that have substituents in the furan ring, the sulfo group enters the benzene ring of the coumarone. Reacting 2-cyanacetylcoumarone with an excess of chlorosulfonic acid at a temperature below +10°, for example, yields the acid chloride of 2-cyanacetylcoumarone-5-sulfo acid (m.p. 130-132°), according to patent specifications [3]. Neither in the patent nor in the scientific literature is there any reference supporting the entrance of the sulfochloride group at the 5 position of the coumarone structure.

2-Cyanacetylcoumarone [4], 2-cyanacetyl-5-benzoylaminocoumarone [5], and a few substituted amides of 2-cyanacetylcoumarone-5-sulfo acid [3,6], prepared by reacting the acid chloride of the latter with various amines, are recommended in the patent literature as components of purple dyes in multilayer color emulsions for photography, [7].

Inasmuch as the literature contains no references to the synthesis of 2-cyanacetylcoumarone-5-sulfo acid or to its structure, other than the patent specifications cited above, we were interested in making a detailed study of this compound, concentrating on the position at which the sulfochloride group enters.

2-Cyanacetylcoumarone was sulfonated with five times its weight of chlorosulfonic acid at 40°. This provided a yield of the sulfochloride as high as 78% of the theoretical. The yield was considerably lower when less chlorosulfonic acid was used or the reaction was carried out at a lower temperature, as specified in the above-cited patent.

We used the method of oxidation with potassium permanganate in an alkaline medium to determine the position where the sulfochloride group entered the coumarone.

There is not much information in the literature on the action of oxidants upon coumarone and its derivatives. It is asserted that coumarone itself is either totally unaffected or is totally decomposed when acted upon by such oxidizing agents as chromic acid and potassium permanganate [8]. On the other hand, the oxidation of 2-cyanacetylcoumarone with potassium permanganate yielded coumarilic acid, coumaroylformic acid being produced under milder conditions (chilling with ice).

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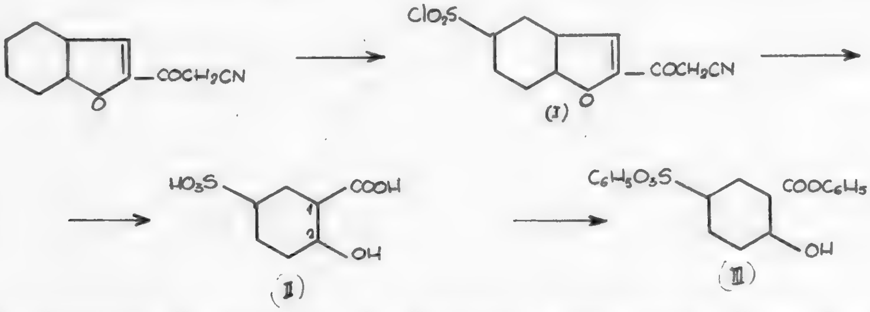
*Deceased.

Our oxidizing of the sulfochloride of 2-cyanacetylcoumarone (I) with potassium permanganate at 3-5° in an alkaline medium yielded 5-sulfosalicylic acid (II), the structure of which was established by converting it into a diphenyl ether (III) by heating it with phenol and phosphorus oxychloride. The resultant compound (III) proved to be the diphenyl ether of 5-sulfosalicylic acid [10].



It may therefore be regarded as definitely established that the sulfochloride group enters at position 5 in the coumarone ring system when 2-cyanacetylcoumarone is reacted with chlorosulfonic acid.

We synthesized the respective anilide and p-toluide of the acid chloride of 2-cyanacetylcoumarone-5-sulfo acid we had prepared.

EXPERIMENTAL

Acid chloride of 2-cyanacetylcoumarone-5-sulfo acid. 18.5 g of 2-cyanacetylcoumarone, with a m.p. of 144-145° (the literature [11] gives the m.p. as 148.5°) was mixed with 93.2 g of chlorosulfonic acid at 40° for 5 hours, after which the reaction mass was poured over 300 g of ice. The resultant precipitate was filtered out, washed with water until its reaction with Congo red was neutral, and dried at 60°. The yield was 78% of the theoretical.

Recrystallization from benzene yielded the sulfochloride as light-yellow prisms. M.p. 134-135° (the patent gives this as 130-132° [3]). Freely soluble in alcohol, acetone, and hot benzene; insoluble in ether and gasoline. Found %: N 4.94, 4.78. $C_{11}H_8O_4NSCl$. Computed %: N 4.93.

Oxidation of the acid chloride and preparation of the diphenyl ether of 5-sulfosalicylic acid. 2.84 g of 2-cyanacetylcoumarone sulfochloride was dissolved in 60 ml of 2 N sodium hydroxide and about 200 ml of a 4% solution of potassium permanganate was added to the solution, with constant stirring, during the course of 3 hours at 3-5°. The filtered solution was evaporated to a volume of 150 ml. The precipitate (a mixture of potassium and sodium chlorides) was filtered out, and the filtrate was again evaporated (to a volume of 60 ml) until elongated needles precipitated out (weight after drying: 4 g). According to a qualitative reaction with ferric chloride (crimson coloring), this substance is a salt of 5-sulfosalicylic acid. The literature describes a diphenyl ether of the latter, prepared by heating a salt of sulfosalicylic acid with phenol and phosphorus oxychloride [10]. We carried out an analogous reaction with our substance for identification purposes. A mixture of the precipitate recovered (4 g) with 3.76 g of phenol and 0.6 g of phosphorus oxychloride was heated to

110-120° for an hour and a half, with constant stirring. The solidified mass was treated with water. The precipitate was filtered out, washed on the filter with cold and hot water, mixed with 30 ml of water, and neutralized with soda. Then the precipitate was again filtered out and dried. Its m.p. was 172-173° after recrystallization from alcohol. The melting point of this substance is the same as that of the diphenyl ether of 5-sulfosalicylic acid. A test sample, mixed with the latter, exhibited no depression of the melting point.

Anilide of 2-cyanacetylcoumarone-5-sulfo acid. A mixture of 2.84 g of the acid chloride of 2-cyanacetylcoumarone-5-sulfo acid, 0.93 g of aniline, and 25 ml of dimethylaniline was stirred for 3 hours at room temperature. The reaction mass was then poured into 70 ml of 18% hydrochloric acid, the resultant precipitate being filtered out and washed with water. Weight: 2.3 g (67.6% of the theoretical). M.p. 80-90°. The substance was purified by recrystallizing it twice from water. Light-yellow crystals, soluble in ethyl alcohol, hot water, and caustic alkali; insoluble in ether or benzene. M.p. 83-84°. Found %: N 8.30. $C_{17}H_{12}O_4N_2S$. Computed %: N 8.21.

p-Toluide of 2-cyanacetylcoumarone-5-sulfo acid. A solution of 2.14 g of p-toluidine in 15 ml of benzene was added to a solution of 2.84 g of the acid chloride of 2-cyanacetylcoumarone-5-sulfo acid, and the mixture was heated over a 60-70° water bath for one hour and over a boiling bath for 15 minutes. The reaction mass was then cooled, the benzene was poured off, and the resultant oil cyrstallized when stirred with ether. The product was filtered out and washed with water. Weight: 1.6 g. An additional 0.9 g of the substance was recovered from the benzene solution by washing the solution with caustic soda and then acidulating it. Total yield: 2.5 g (70.4% of the theoretical). The substance was purified by recrystallizing it twice from 80% acetic acid. Light yellow prisms. Freely soluble in alcohol, caustic alkali, and hot acetic acid, less so in benzene; soluble in ether. M.p. 126-127°. Found %: N 7.66. $C_{18}H_{14}O_4N_2S$. Computed %: N 7.89.

SUMMARY

1. It has been found that reacting 2-cyanacetylcoumarone with chlorosulfonic acid causes the sulfochloride group to enter the coumarone ring structure at the 5-position.

2. The optimum conditions have been found for sulfonating 2-cyanacetylcoumarone by chlorosulfonic acid (using an excess of five times the weight of chlorosulfonic acid at 40°). Under these conditions the yield of the acid chloride of 2-cyanacetylcoumarone-5-chlorosulfo acid is as high as 78% of the theoretical.

3. The anilide and toluide of 2-cyanacetylcoumarone-5-sulfo acid have been synthesized.

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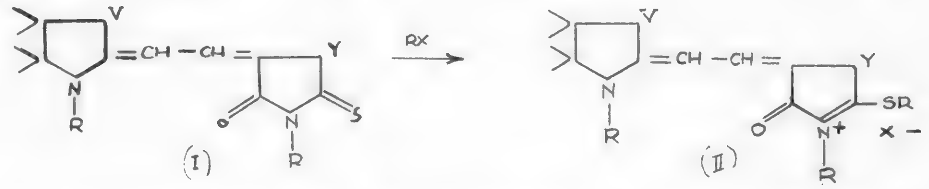
MEROCYANIN DYES THAT ARE DERIVATIVES OF RHODANINE

I. THE PROPERTIES OF THE METHYL-METHYL SULFATE OF 2-METHYLMERCAPTO-5-(3'-ETHYL-BENZOTHIAZOLINYLIDENE-2'-ETHYLIDENE)-THIAZOLINONE-4

Z. P. Sytnik, I. I. Levkoyev and M. V. Deichmeister

When alkylating agents act upon merocyanins (I) that contain a thiocarbonyl group linked to a nitrogen atom, quaternary salts of structure (II) are easily formed:

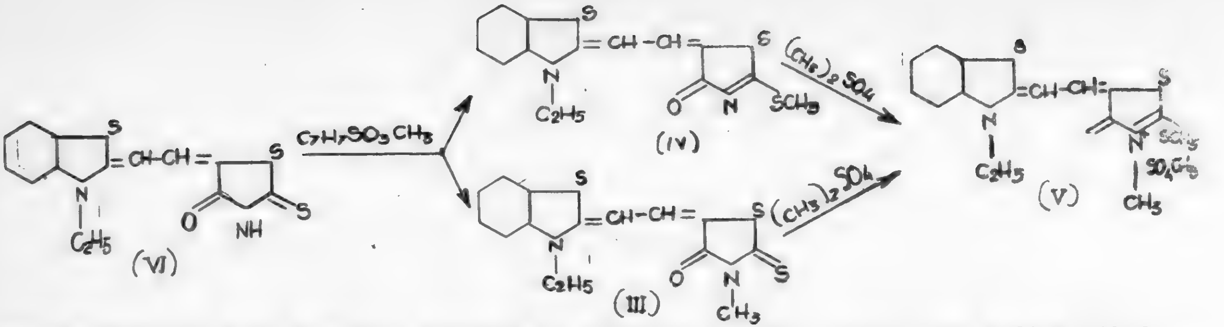


where R is an alkyl; V is O, S, Se, CH=CH, $C(CH_3)_2$; Y is O, S, Se, NH; and X is an acid group.

These compounds have been described only in the patent literature, as intermediates in the synthesis of the rhodacyanins [1], during which they cannot be isolated in the pure state. According to the specifications of one of these patents [2], the quaternary salts of merocyanin derivatives (II, Y = S) are freely soluble in water, in contrast to the merocyanins, and are more light-sensitive.

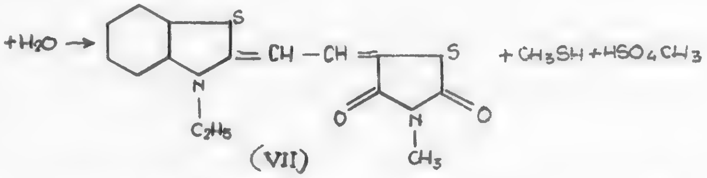
In synthesizing rhodacyanin dyes we noticed that the quaternary salts of the merocyanin derivatives of rhodanine decompose readily. This led us into a more detailed investigation of the properties of these compounds. In the present paper we have made a study of the synthesis and the properties of the methyl-methyl sulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (V). According to the patent specifications [3], this salt can be synthesized by heating the respective merocyanin (III) with dimethyl sulfate. This compound should also result from the action of dimethyl sulfate upon the merocyanin (IV). We have shown that satisfactory yields of the same quaternary salt (V) can be secured by heating either of these merocyanins (III or IV) with dimethyl sulfate.

The merocyanin (IV) was synthesized by methylating 5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one 4 (VI) with the methyl ester of p-toluenesulfo acid and potassium hydroxide in alcohol [4]. We found that in addition to the 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV), an isomeric dye (III) was formed as a product of the methylation of the merocyanin (VI) at the nitrogen atom. But when the merocyanin (VI)



was methylated with dimethyl sulfate in absolute alcohol containing sodium ethylate, no N-methyl derivative (III) was found, the 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV) being secured in the pure state. Thus, the methylation of 5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 (VI) may occur at the sulfur atom or at the nitrogen atom, depending upon the reaction conditions and corresponding to two tautomeric forms of the original merocyanin. The instability of the synthesized quaternary salt was manifest even during its refining. When this compound was recrystallized from ethyl alcohol, copious quantities of methanethiol were evolved, and orange crystals, whose properties differed sharply from those of the original merocyanin, settled out of the filtrate together with the quaternary salt. The quaternary salt is highly soluble in water, a precipitate slowly settling out of the bluish-red solution. This hydrolysis is greatly accelerated by heating, the solution being nearly completely decolorized after heating for 2 hours. The precipitated orange dye is freely soluble in benzene and ether, in which the quaternary salt does not dissolve. It possesses the typical properties of the merocyanins, its absorption maximum in alcoholic solution being sharply shifted toward the short-wave end of the spectrum, as compared to the quaternary salt and the merocyanins (III) and (IV). These properties, as well as the chemical analysis of the synthesized compound, indicate that the quaternary salt (V) hydrolyzes readily evolving methanethiol and giving rise to a merocyanin with a 3-methylthiazolidinedione-2,4 group, (VII):

Salt (V)



(VII)

This process is analogous to the hydrolysis of the quaternary salts of a 2-alkylmercaptobenzothiazole [5,6]; hydrolysis of the type (V) salts takes place with extraordinary ease, however.

We have measured the absorption curves of alcoholic solutionsof the merocyanins (III), (IV), (VI), and (VII) and of the quaternary salt (V). The measurements were made with a Koenig-Martens spectrophotometer. The absorption maxima of these dyes are listed in the subjoined table.

As we see from this table, the position of the absorption maximum remains practically unchanged as we pass from the merocyanin of the unsubstituted rhodanine (VI) to the N-methyl derivative (III). 2-Methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV), which differs from the merocyanin (III) by having a different tautomeric form of the rhodanine group, exhibits a perceptible bathochromic effect. The formation of the quaternary salt (V) produces a much deeper color than that of the original merocyanins. When the

Dyestuff	Absorption maximum, mμ
5-(3'-Ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 (VI)	520
3-Methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 (III)	522
2-Methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV)	526
Methyl-methyl sulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (V)	536
3-Methyl-5-(3'-ethylbenzothiazolinylidine-2'-ethylidene)-thiazolidinedione-2,4 (VII)	464

sulfur atom in the 2 position of the thiazolidine group is replaced by an oxygen atom (VII), a marked hypsochromic effect is observed (58 mμ). A merocyanin with an unsubstituted rhodanine group (VI) and its N-methyl derivative (III) sensitize silver bromide to the yellow and green portions of the spectrum rather weakly. 2-Methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV) is somewhat more effective. On the other hand, the sensitizing effect of a merocyanin with a thiazolidinedione group is much less than that of the dyes (VI) and (III). The quaternary salt (V) is a weak sensitizer, lowering the aggregate sensitivity of the silver bromide emulsion perceptibly.

EXPERIMENTAL

5-(Acetanilinomethylene)-rhodanine. A solution of 1.33 g of rhodanine and 1.96 g of diphenylformamidine in 15 ml of acetic anhydride was boiled for 1 hour. The next day the resultant precipitate was filtered out and washed with water and with alcohol. Weight: 2.35 g. The product was recrystallized from 135 ml of alcohol to purify it. Weight: 1.94 g (70% of the theoretical). Yellow needles, with a m.p. of 240-242°.

Found %: S 22.85, 22.98. $C_{12}H_{10}O_2N_2S_2$. Computed %: S 23.02.

3-Methyl-5-(acetanilinomethylene)-rhodanine. Like the preceding product, this was prepared from 1.47 g of 3-methylrhodanine and 1.96 g of diphenylformamidine. The yield was 1.88 g (64.4% of the theoretical) after recrystallization from alcohol (1 g from 50 ml). Golden lamellae with a m.p. of 166-168°.

5-(3'-Ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 (VI). A mixture of 0.56 g of 5-(acetanilinomethylene)-rhodanine, 0.67 g of 2-methylbenzothiazole ethiodide, and 10 ml of pyridine was heated to 130° over an oil bath for 15 minutes. Several hours later the precipitate was filtered out and washed on the filter with water, alcohol, and ether. Weight: 0.33 g. The resultant dye is extremely slightly soluble in alcohol (1 g in 20 liters of boiling alcohol) or in benzene; it is readily soluble in pyridine and in glacial acetic acid. Washing twice with boiling alcohol (25 ml each time) yielded a pure product with a m.p. of 276° (with decomposition). Weight: 0.32 g (50% of the theoretical). The sample was recrystallized from an alcohol-pyridine mixture (1 g to 1200 ml of a 4:1 mixture). Minute violet needles with a m.p. of 276° (with decomposition).

Found %: N 8.66. $C_{14}H_{12}ON_2S_3$. Computed %: N 8.74.

3-Methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 (III). This was prepared like the preceding dye, from 0.58 g of 3-methyl-

5-(acetanilinomethylene)-rhodanine and 0.67 g of 2-methylbenzothiazole ethiodide in 10 ml of pyridine. The yield of the pure dye, recrystallized from alcohol (1 g to 4 liters), was 0.34 g (50% of the theoretical). Dark red, minute needles with a m.p. of 268-269° (with decomposition).

Found %: N 8.48. $C_{15}H_{14}ON_2S_3$. Computed %: N 8.37.

2-Methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 (IV). This dye was synthesized in two ways: 1) 0.16 g of potassium hydroxide and 0.44 g of the methyl ester of *p*-toluenesulfo acid were added to a suspension of 0.64 g of 5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 in 10 ml of alcohol, and the mixture was then heated for 20 minutes over a boiling water bath. The next day the precipitate was filtered out and washed with water and with alcohol. Weight: 0.51 g. The product was boiled with 350 ml of ethyl alcohol, and the hot solution was filtered (the precipitate weighed 0.09 g, with a m.p. of 255-257° with decomposition) and chilled. Double recrystallization from benzene yielded the product as 0.15 g (22% of the theoretical) of red-violet needles with a m.p. of 249-251° (with decomposition).

Found %: N 8.44. $C_{15}H_{14}ON_2S_3$. Computed %: N 8.37.

The dye (m.p. 256-257°), which was insoluble in alcohol, was crystallized from benzene. Yield: 0.05 g; m.p. 268° (with decomposition). A test sample of this dye, mixed with 3-methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4, produced by a different method (*vide infra*), exhibited no depression of the melting point. The absorption curves of the two dyes were likewise identical.

2) 0.8 g of 5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 was dissolved in 7 ml of absolute alcohol containing 0.17 g of sodium ethylate, and 0.33 g of dimethyl sulfate was added slowly drop by drop, with vigorous agitation. The resultant pasty mass was heated to 60° for 20 minutes. After it had cooled, the precipitate was filtered out and washed with water and alcohol. The somewhat tarry product (0.8 g) was boiled with 120 ml of ethyl alcohol, and the insoluble residue filtered out, crystallized from 450 ml of ethyl alcohol (yield 0.40 g) and then twice recrystallized from benzene. Yield 0.28 g (33.7% of theory). Minute red-violet needles, m.p. 249-251° (decomp) No m.p. depression when mixed with the dye synthesized by the first method. The absorption maxima of the two dyes were likewise identical (526 mμ).

Methyl-methyl sulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)thiazolinone-4 (V). This quaternary salt was synthesized by two methods:

1) 0.33 g of 3-methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion 2-one-4 and 0.378 g of dimethyl sulfate were heated for 15 minutes to 130° (temperature within the mixture). After it had cooled, the quaternary salt was first washed with absolute ether and then boiled twice with anhydrous benzene (using 25 ml each time). Yield: 0.42 g (90% of the theoretical) Dark-red needles, freely soluble in water, alcohol, and chloroform, and insoluble in benzene or ether. M.p. 211-212° (with decomposition).

Found %: N 5.96. $C_{17}H_{20}O_5N_2S_4$. Computed %: N 6.07.

2) 0.33 g of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 and 0.378 g of dimethyl sulfate were heated together for 2 hours to 110° (temperature within the mixture). The resultant product was washed with absolute ether and then washed twice with boiling benzene (using 25 ml each time). Yield: 0.29 g (63% of the theoretical). M.p. 211-212° (with decomposition). The properties of this dye indicated its identity with the product synthesized by Method 1, nor did it exhibit any depression of the melting point

when mixed with the latter.

3-Methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinedione-2,4 (VII). [Decomposition of the quaternary salt (V) in an aqueous medium]. A solution of 0.02 g of the methyl-methyl sulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 in 20 ml of water was boiled for two hours. As boiling continued, large quantities of methanethiol were evolved, and an orange precipitate settled out. After the mixture had cooled, the precipitate was filtered out and washed with water and alcohol. Yield: 0.58 g (92% of the theoretical); m.p. 247-249° (with decomposition). The melting point of the dye did not change after it had been recrystallized from 150 ml of alcohol. Yellow-orange needles; rather freely soluble in alcohol, benzene, and ether; insoluble in water.

Found %: S 19.97. $C_{15}H_{14}O_2N_2S_2$. Computed %: S 20.15.

We wish to express our profound gratitude to C.V.Natanson, under whose direction the spectrophotometric measurements, as well as the investigations of the photographic properties of these dyes, were made.

SUMMARY

1. The methyl-methyl sulfate of 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 has been synthesized by reacting 3-methyl-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 or 2-methylmercapto-5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolinone-4 with dimethyl sulfate. It has been found that heating this compound in water or in an aqueous-alcoholic medium hydrolyzes it completely, methanethiol being evolved and a merocyanin with a thiazolidinedione-2,4 group being formed.

2. It has been shown that 5-(3'-ethylbenzothiazolinylidene-2'-ethylidene)-thiazolidinethion-2-one-4 can be methylated at the sulfur atom or at the nitrogen atom, depending upon the reaction conditions and corresponding to the two tautomeric forms of the original merocyanin.

3. A study has been made of the optical and photographic properties of the synthesized dyes.

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ALKALOIDS OF SOME SPECIES OF THE LEGUME FAMILY

X. NEW ALKALOIDS FROM PIPTANTHUS NANUS M. POP. - PIPTANTINE AND PIPTAMINE

R. A. Konovalova, B. S. Diskina and M. S. Rabinovich

This research is a continuation of a series of papers dealing with the alkaloids of species of the legume family that grow in the USSR.

All the representatives of this family investigated up to now are plants that are extremely rich in alkaloids. This fact, together with the appreciable toxicity and wide distribution of numerous botanical species of the legume family, justifies a rather thoroughgoing investigation of the alkaloids of this group.

Table 1 lists the results of the exploration of some of the species of the legume family that grow in the Soviet Union.

We see from the data in Table 1 that Soviet research workers have isolated from various species of the Leguminosaceae family nine new alkaloids; pachycarpine, sophoridine, sophocarpine, sophoramine, aloperine, thermopsine, homothermopsine, ammodendrine, isoammodendrine, and ammothamnine, in addition to other bases that had already been described in the literature: matrine, anagyrine, lupanine, sparteine, cytisine, and methylcytisine.

The plant used in the present investigation was the botanical species Piptanthus nanus* (family Leguminosaceae), which grows in the Tien Shan region. It was first discovered by the Russian botanist M. Popov in 1931 in Kashgaria. In 1946 P.n. was found in the Kokomeren Pass (in the Central Tien Shan) by P.S. Massagetov, the head of an expedition of the All-Union Research Institute of Pharmaceutical Chemistry, who was the first to establish the alkaloid properties of this plant and to suggest that it be subjected to further chemical investigation. P.n. proved to be extraordinarily rich in alkaloids, which total 2.5% of the dry weight of the plant. The bases were recovered from the parts of the plant above ground in the usual manner - extraction with dichloroethane, followed by leaching with dilute acid. The alkaloids could be separated by making use of their different basicities and the different solubilities of their nitrates in acetone. This yielded three alkaloids, one a liquid and the other two crystalline.

The liquid base represents nearly half the total alkaloids recovered from the mother liquor after the crystalline alkaloids had been filtered out, or 1.1%, by weight of the plant. It is a light-yellow oil that darkens when exposed to the air, with a b.p. of 138-140° (at 4 mm), a levorotatory, dibasic, tertiary base, which forms well-crystallized salts: a dihydroiodide, a dipicrate, and a crystalline monomethiodide. The salts resemble l-sparteine in all their properties and constants.

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* Henceforth abbreviated to P.n.

TABLE 1

No.	Botanical species	Alkaloids isolated		Composition	Researchers
		Described in the literature	New		
1	Sophora pachycarpa	–	Pachycarpine	$C_{15}H_{26}N_2$	A.P.Orekhov, M.S. Rabinovich, R.A. Konovalova [1]
		–	Sophocarpine	$C_{15}H_{24}ON_2$	A.P.Orekhov, N.F. Proskurnina [2]
		Matrine	–	$C_{15}H_{24}ON_2$	
2	Sophora alopecuroides....	–	Sophoridine	$C_{15}H_{26}ON_2$	A.P.Orekhov [3]
		–	Sophoramine	$C_{15}H_{20}ON_2$	
3	Sophora flavescens	–	Aloperine	$C_{15}H_{24}N_2$	A.P.Orekhov, N.F. Proskurnina, and R.A.Konovalova [4]
		–	Sophocarpine	$C_{15}H_{24}ON_2$	
		Matrine	–	$C_{15}H_{24}ON_2$	
4	Thermopsis lanceolata,......	–	Thermopsine	$C_{15}H_{20}ON_2$	A.P.Orekhov and E.L.Gurevich, [5,6]
		–	Pachycarpine	$C_{15}H_{26}N_2$	
		–	Homothermopsine	$C_{17}H_{24}ON_2$	
		Anagyrine	–	$C_{15}H_{20}ON_2$	
		Methylcytisine	–	$C_{12}H_{16}ON_2$	
5	Ammodendron Conollyi.........	–	Ammodendrine	$C_{12}H_{22}ON_2$	A.P.Orekhov, N.F. Proskurnina [7]
		–	Pachycarpine	$C_{15}H_{26}N_2$	
		–	Isoammodendrine	$C_{12}H_{22}ON_2$	V.M.Merlis and Proskurnina [8]
6	Cytisus caucasicus	Lupanine	–	$C_{15}H_{24}ON_2$	A.P.Orekhov [9]
		–	Pachycarpine	$C_{15}H_{26}N_2$	
7	Cytisus ratisbonensis	Lupanine	–	$C_{15}H_{24}ON_2$	A.P.Orekhov [10]
		Sparteine	–	$C_{15}H_{26}N_2$	
8	Genista tinctoria	Cytisine	–	$C_{11}H_{14}ON_2$	A.P.Orekhov and T.Narkuziev [11]
		Methylcytisine	–	$C_{12}H_{16}ON_2$	
		Anagyrine	–	$C_{15}H_{20}ON_2$	
9	Ammonthamnus Lehmanni Bge	Pachycarpine	–	$C_{15}H_{26}N_2$	A.Sadikov and G.Lazuryevsky [12]
		Sophocarpine	–	$C_{15}H_{24}ON_2$	
		–	Ammothamnine	$C_{15}H_{24}O_3N_2$	

As we see from the data in Table 2, a direct comparison of the two alkaloids proved they were identical.

The properties of the crystalline alkaloids isolated from P.n. differ from those of all alkaloids described up to now, thus entitling us to name then piptantine and piptamine, respectively. Piptantine is a weakly basic alkaloid that is recovered from the salt solutions by the action of sodium bicarbonate. It crystallizes readily from acetone and ether, fuses at 143.5-144.5°, rotates the plane of polarization to the left $[\alpha]_D$ -24.3°, and forms a number of crystalline salts: the hydrobromide, the hydrochloride, and the nitrate, which is very

TABLE 2

	Base isolated from *Piptanthus nanus*	l-Sparteine	Melting point of mixed test sample
Boiling point	138-140° (4 mm)	188-190° (18 mm)	-
Dihydriodide (m.p.)...	255-257°	257-258°	256-257°
Picrate (m.p.)	198-199	208	198-199
Monomethiodide (m.p.).	236-237	236-238	-
$[\alpha]_D$ in alcohol	-15.6	-16.3	-

slightly soluble in acetone. Ultimate analysis of the base as well as of its salts indicates that the formula of piptantine is $C_{14}H_{24}N_2$. No N-alkyl groups were found, and the pyrrole reaction was negative.

When piptantine is heated with methyl iodide, the hydriodide is formed, decomposing when exposed to a 25% ammonia solution. This results in the formation of a new crystalline base with a m.p. of 111-112°, which exhibits a depression of the melting point when mixed with the original piptantine. Ultimate analysis and determination of the N-alkyl group indicate that this base is N-methylpiptantine. When piptantine is reacted with acetic anhydride (in pyridine), a new crystalline base, with a m.p. of 213-215° is formed; its ultimate analysis indicates that it is the monoacetyl derivative of piptantine. The latter was unaffected by heating with methyl iodide. Finally, when reacted with sodium nitrate, piptantine yields a nitroso derivative that exhibits a pronounced positive Liebermann reaction. All these properties of piptantine testify to that alkaloid's possessing one atom of secondary nitrogen.

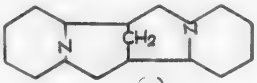
Piptamine is a stronger base than piptantine. The only way to recover it from its salt solutions is with ammonia. It crystallizes readily from acetone, fuses at 173-174°, and is optically inactive. It forms a readily crystallizable hydrochloride and hydrobromide. It differs from piptantine in that its nitrate dissolves very freely in acetone, thus making possible the complete separation of the two alkaloids.

Ultimate analysis of the base and of its hydrochloride indicates that the formula for the base is $C_{14}H_{24}N_2$, i.e., it is an isomer of piptantine. It, too, has no N-alkyl group, and its pyrrole reaction is negative.

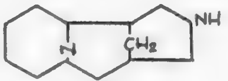
When piptamine is heated with methyl iodide, a hydriodide results, which is decomposed by a 25% solution of ammonia. This, in turn, yields a new crystalline base, with a m.p. of 96-97°, which exhibits a depression of the melting point when mixed with the original piptamine. Ultimate analysis indicates that this base is N-methylpiptamine. The action of acetic anhydride on piptamine (in pyridine) yields a new crystalline base, with a m.p. of 92-96°, which is the monoacetyl derivative of piptamine according to its ultimate analysis. When piptamine is reacted with sodium nitrite, a nitroso derivative is formed, which exhibits a marked positive Liebermann reaction. All these properties of piptamine testify to the presence of a single atom of secondary nitrogen in that alkaloid. Moreover, our study of piptamine indicates its great resemblance to piptantine, which justifies our regarding the two as an instance of optical isomerism.

The two new crystalline secondary bases with the composition of $C_{14}H_{24}N_2$ isolated from the legume family are doubtless of great interest. As we see from Table 1, the overwhelming majority of alkaloids of this group isolated in our laboratory up to now belong to the C_{15} series. The ancestors of this series are pachycarpine and sparteine, the molecules of which possess a complicated heterocyclic system that contains two condensed quinolizidine (lupinane) rings (I).

Cytisine, with the formula $C_{11}H_{14}ON_2$ (II), is directly related to this system, since it also has a quinolizidine group.

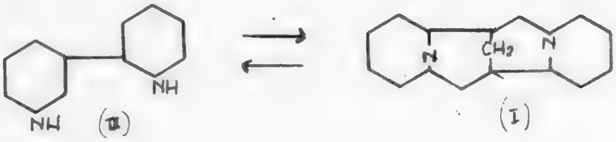


(I)



(II)

Ammodendrine (and isoammodendrine), with the formula $C_{12}H_{22}ON_2$, which are found in various Ammodendron species together with pachycarpine, is very probably structurally related to the latter. This hypothesis, put forward by the late Academician A.P.Orekhov, is supported by the fact that the relative amount of both alkaloids varies greatly in Ammodendron during the various seasons. One of these structural types must therefore be converted into the other within the plant:



An extremely interesting problem is the relationship between the two alkaloids newly isolated, piptantine and piptamine, and the sparteine that is found together with them. The fact that these new bases contain one less carbon atom than sparteine leads one to wonder whether they are not intermediate products, formed during the plant's synthesis of sparteine.

Our study of the structure of piptantine and piptamine is being continued.

EXPERIMENTAL

Recovery of the alkaloids. 8.5 kg of the parts of the plant Piptanthus nanus that grow above the ground were wetted with a 10% ammonia solution and exhaustively extracted with dichloroethane. The dichloroethane extracts were repeatedly extracted with 10% sulfuric acid. The acid solutions were alkalinized with a 25% ammonia solution and then extracted successively with ether and chloroform. The ether was driven off, the 180 g of residue being a dark, viscous mass After the solvent had been driven off from the chloroform extract, we had left 43 g of an alkaloid mixture as a tarry mass.

Separation of the bases. 180 g of the alkaloid mixture, secured by extraction with ether, was dissolved in 10% sulfuric acid. The acid solution was washed a few times with chloroform, and then sodium bicarbonate was added until its litmus reaction was alkaline. The alkaline solution was exhaustively extracted with ether and then with chloroform. The ether solution was desiccated above sodium sulfate and then evaporated, the residue (56 g) consisting of a viscous, dark, oily liquid, from which 23.1 g of a colorless crystalline base with a m.p. of 136-140° was recovered by trituration with acetone. We named the alkaloid piptantine. The aqueous solution of the bases left after the ether extraction was alkalinized with an excess of 25% ammonia and then exhaustively extracted with ether. The ether solution was desiccated above sodium sulfate and then evaporated; acetone was added to the residue, which was a thick, dark oil weighing 115 g; trituration of the latter with the acetone yielded 7.6 g of a crystalline base with a m.p. of 162-163°. We named the alkaloid piptamine.

The acetone was driven out of the mother liquors left after filtration of the crystalline bases, which still contained a large quantity of alkaloids, and then the residue was fractionated in vacuum. The 33 g of the mixture of bases, which was a dark, tarry mass, was distilled in a 4-mm vacuum, the following two fractions being collected: I – b.p. 143-155°, 22 g of a light-yellow, highly mobile oil with a disagreeable odor, which darkened upon exposure to the air, a tar separating out; and II – b.p. 190-210°, 6 g of a light-yellow hyaline mass that solidified rapidly.

Fraction I. Specific rotatory power: 1.1468 g of the substance in 15 ml of ethyl alcohol ($\underline{l}$ 1 dm); α_D -1.19°; $[\alpha]_D$ -15.6°.

The picrate was prepared by mixing alcoholic solutions of the base and of picric acid. It settled out as a yellow crystalline precipitate. Its m.p. was 198-199° after recrystallization from acetone. A test sample, mixed with the picrate of l-sparteine, had a m.p. of 198-199°.

Monomethiodide. 10 g of the base was dissolved in 14 g of ethyl acetate. The resulting solution was heated for 3 hours on a water bath with 13 g of methyl iodide. After the solution had cooled, colorless crystals settled out, which were dissolved in 40 ml of chloroform. To this solution 40 ml of hot ethyl acetate was added, causing a colorless crystalline substance to settle out. The resultant methiodide was recrystallized from water and then had a m.p. of 236-237° (the m.p. of the methiodide of l-sparteine is 236-238°).

Dihydriodide. 7 g of potassium iodide was added to 5 g of the base dissolved in 30 ml of 10% sulfuric acid. The light yellow crystals of the dihydriodide that settled out of the solution were filtered out, washed with acetone, and recrystallized from water. The resulting dihydriodide had a m.p. of 255-257°. A test sample mixed with the dihydriodide of l-sparteine, fused at 256-257°.

Fraction II. The base was triturated with acetone, a white crystalline precipitate settling out; it had m.p. of 171-173° after recrystallization from acetone. A test sample, mixed with the alkaloid piptamine, fused at 171-173°.

Piptantine nitrate was prepared by adding nitric acid diluted with acetone to the base in acetone. The product was recrystallized from aqueous alcohol. Acicular crystals with a m.p. of 205-206°. The nitrate is insoluble in acetone or ethyl alcohol, but is freely soluble in water.

3.685 mg substance: 6.216 mg CO_2; 2.640 mg H_2O. 3.833 mg substance: 6.500 mg CO_2; 2.695 mg H_2O. 4.750 mg substance: 0.684 ml N_2 (26°, 727 mm). Found %: C 46.00, 46.24; H 8.02, 7.87; N 15.68. $C_{14}H_{24}N_2 \cdot 2HNO_3 \cdot H_2O$. Computed %: C 46.16; H 7.7; N 15.38. 0.0714 g substance: in 4 ml of water ($\underline{l}$ 0.5 dm); α_D -0.03°; $[\alpha]_D$ -3.3°.

The piptantine base was isolated by decomposing the nitrate by adding 25% ammonia to an aqueous solution of the latter. It was recrystallized from acetone. Lamellar needles, with a m.p. of 143.5-144.5°. Recrystallization caused no change in the melting point.

3.699 mg substance: 10.384 mg CO_2; 3.600 mg H_2O. 3.235 mg substance: 9.060 mg CO_2; 3.227 mg H_2O. 3.485 mg substance; 0.397 ml N_2 (21.5°, 736.5 mm). 4.739 mg substance: 0.551 ml N_2 (26°, 728.0 mm). Found %: C 76.55, 76.33; H 10.89, 11.16; N 12.85, 12.71. M 238 (Rast). $C_{14}H_{24}N_2$. Computed %: C 76.37; H 10.90; N 12.72. M 220. 0.1090 g substance: in 5 ml ethyl alcohol ($\underline{l}$ 0.5 dm); α_D -0.265°; $[\alpha]_D$ -24.3°.

Wilstätter reaction: a solution of the base in sulfuric acid did not decolorize permanganate.

Pyrrole reaction: When the base was heated with zinc dust, a pine chip soaked in concentrated HCl and held in the vapor did not turn red.

The hydrochloride was prepared by adding an alcoholic solution of HCl to the base in acetone. It was recrystallized from absolute alcohol. Rhombic crystals with a m.p. of ~256° with decomposition.

0.2479 g in 5 ml of water ($\underline{l}$ 0.5 dm); α_D -0.03°; $[\alpha]_D$ -1.21°.

5.295 mg substance: 4.419 mg AgCl. 7.952 mg substance: 7.386 mg AgCl. Found %: Cl 22.98, 22.98. $C_{14}H_{24}N_2 \cdot 2HCl \cdot H_2O$. Computed %: Cl 22.83.

The hydrobromide was prepared by adding an aqueous solution of hydrobromic acid (65%) to the base in acetone. The minute needles had a m.p. of 286° (with decomposition) after recrystallization from ethyl alcohol.

0.2290 g substance: in 5 ml of water ($\underline{l}$ 0.5 dm); α_D -0.04°; $[\alpha]_D$ -1.72°. 6.923 mg substance: 6.623 mg AgBr. Found %: Br 40.71.
$C_{14}H_{24}N_2 \cdot 2HBr \cdot H_2O$. Computed %: Br 39.97.

Action of methyl iodide on piptantine. 2 g of the base was dissolved in 25 ml of ethyl acetate and then heated for 30 minutes over a water bath with 3 g of methyl iodide. Silky acicular crystals were thrown down at once from the boiling solution. The hydriodide had a m.p. of 238-239° after recrystallization from water.

N-Methylpiptantine was prepared by adding an excess of 25% ammonia to an aqueous solution of the hydriodide. The white precipitate, which was insoluble in water, was recrystallized from acetone as lamellar needles, with a m.p. of 111-112°. A test sample, mixed with piptantine, fused at 102-106°.

4.591 mg substance: 0.487 ml N_2 (19.5°, 736.1 mm). 5.376 mg substance: 6.97 ml 1/50 $\underline{N}$ $Na_2S_2O_3$. Found %: N 11.99. NCH_3 12.54. $C_{14}H_{23}N_2CH_3$. Computed %: N 11.96, NCH_3 12.38. 0.0863 g substance: in 4 ml ethyl alcohol ($\underline{l}$ 0.5 dm); α_D -0.08°; $[\alpha]_D$ -7.42°.

The nitrate of N-methylpiptantine was prepared by adding nitric acid (sp. gr. 1.42) diluted with acetone to the base in acetone. It had a m.p. of 157-158° after recrystallization from ethyl alcohol.

N-Acetylpiptantine. 0.5 g of the base was dissolved in 5 ml of acetic anhydride and heated for 5 hours with 2 ml of pyridine over a water bath. The excess acetic anhydride was decomposed with water, and 25% ammonia was added to the solution. A white precipitate settled out, which was recrystallized from acetone. Minute globular crystals with a m.p. of 213-215°.

4.342 mg substance: 0.392 ml N_2 (16°, 747.6 mm). 4.807 mg substance: 0.431 ml N_2 (16°, 742.6 mm). Found %: N 10.52, 10.36.
$C_{14}H_{23}N_2COCH_3$. Computed %: N 10.68.

Nitrosopiptantine was prepared by slowly adding a 10% aqueous solution of sodium nitrite, with chilling, to a solution of the base in dilute hydrochloric acid. Neutralization with alkali threw down a white precipitate that was freely soluble in ether, acetone, benzene, and alcohol, but was insoluble in water. It did not have a sharp melting point, decomposing at 95°. It exhibited an intense positive Lieberman reaction.

Piptamine. The base was recrystallized from acetone (1:100). Minute cubic crystals with a m.p. of 173-174°. Recrystallization did not raise the melting point. The base is slightly soluble in acetone, insoluble in water, and freely soluble in ether and alcohol. The nitrate of the base is soluble in alcohol and acetone.

3.110 mg substance: 8.729 mg CO_2; 3.081 mg H_2O. 2.672 mg substance: 7.479 mg CO_2; 2.600 mg H_2O. 4.066 mg substance: 0.473 ml N_2 (21.5°, 732 mm). Found %: C 76.54, 76.25; H 11.08, 10.88; N 12.98; M 218.4 (Rast). $C_{14}H_{24}N_2$. Computed %: C 76.37; H 10.90; N 12.72; M 220.

An alcoholic solution of the base is optically inactive.

Wilstätter reaction: a solution of the base in sulfuric acid did not decolorize a permanganate solution.

Pyrrole reaction: When the base was heated with zinc dust, a pine chip wetted with concentrated HCl and held in the vapor did not turn red.

The hydrochloride was prepared by adding an alcoholic solution of HCl to the base in acetone. Its melting point was ~ 335° (with decomposition) after recrystallization from a mixture of acetone and alcohol.

6.482 mg substance: 6.311 mg AgCl. 4.930 mg substance: 4.817 mg AgCl. Found %: Cl 24.09, 24.17, $C_{14}H_{24}N_2 \cdot 2HCl$. Computed %: Cl 24.23.

The hydrobromide was prepared by adding an aqueous solution of hydrobromic acid to the base in acetone. The m.p. was ~ 294° (with decomposition) after recrystallization from ethyl alcohol.

Action of methyl iodide on piptamine. 0.4 g of the base was dissolved in 15 ml of ethyl acetate and then heated for 40 minutes with 0.5 g of methyl iodide over a water bath. A crystalline precipitate, which proved to be a mixture of the hydriodides of the original and the methylated bases, settled out soon after heating had begun. The 0.52 g of the hydriodide was treated with boiling ether and then decomposed with 25% NH_4OH. The precipitated base dissolved completely in ether. The ether was driven off, and the residue was recrystallized from acetone, the base that crystallized out having a m.p. of 168-174° and exhibiting no depression of the melting point when mixed with the original base. A new base with a m.p. of 93-96° was recovered from the acetone mother liquor; in contrast to the original base, its nitrate was insoluble in acetone. The base was isolated from the nitrate and recrystallized from acetone; its m.p. then was 96.5-97.5°.

5.210 mg substance: 0.555 ml N_2 (16.5°, 741.4 mm). Found %: N 12.24. $C_{14}H_{23}N_2 \cdot CH_3$. Computed %: N 11.96.

N-Acetylpiptamine. 0.5 g of the base was dissolved in 5 ml of acetic anhydride and then heated for 6 hours with 2 ml of pyridine over a water bath. The excess acetic anhydride was decomposed with water, and 25% ammonia was added to the solution. The precipitated base was extracted with ether. The extract was desiccated above Na_2SO_4, the ether was driven off, and the residue was recrystallized from acetone. M.p. 92-96° (with decomposition).

4.680 mg substance: 0.441 ml N_2 (19°, 736 mm). Found %: N 10.66. $C_{12}H_{23}N_2 \cdot COCH_3$. Computed %: N 10.68.

Nitrosopiptamine was prepared by slowly adding a 10% aqueous solution of sodium nitrite, with chilling, to a solution of the base in dilute hydrochloric acid. Neutralization with alkali threw down a white precipitate that was freely soluble in alcohol, ether, acetone, and benzene, but insoluble in water. We were unable to recrystallize it. The compound exhibited an intense positive Liebermann reaction.

SUMMARY

1. A study has been made of the Central Asian botanical species Piptanthus nanus M. Pop. of the legume family, which has proved to be a plant extremely rich

in alkaloids. The aggregate alkaloids recovered total 2.5% of the weight of the dry plant.

2. Separation of the total alkaloids has yielded three alkaloids; a liquid base, $C_{15}H_{26}N_2$, identified as l-sparteine, and two new crystalline alkaloids, $C_{14}H_{24}N_2$, which have been named piptantine and piptamine.

3. The secondary nature of one of the nitrogen atoms in the molecule of these two alkaloids has been established by the preparation of their N-methyl-N-acetyl, and nitroso derivatives.

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*See CB translation p. 1781 ff.

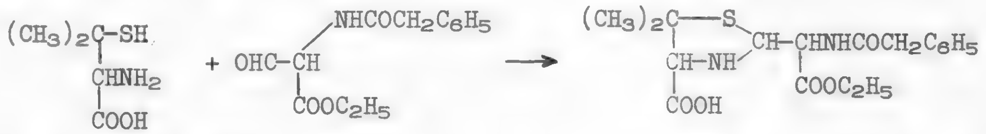
INTRODUCTION OF A FORMYL GROUP INTO ACYL AMINO ACIDS AND CONDENSATION OF THE RESULTING COMPOUNDS WITH THIOLAMINO ACIDS TO FORM THIAZOLIDINE DERIVATIVES

II. THE α-FORMYLPHENACETURIC ESTER AND ITS DERIVATIVES

A. S. Elina and O. Yu. Magidson

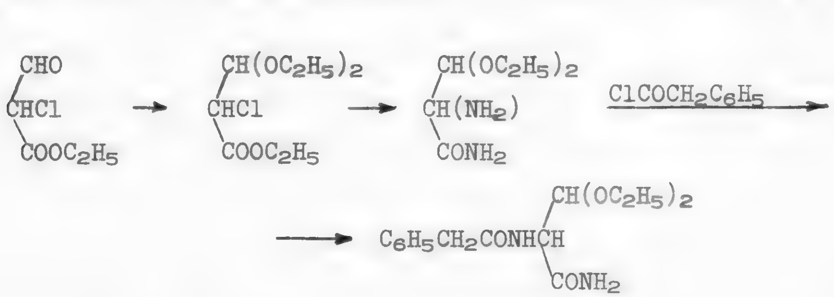
In our preceding report we described the synthesis of an analog of ethyl penicilloic ester, viz.: the ethyl ester of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-hippuric acid.

The goal of the present investigation was the synthesis of the ethyl ester of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic acid, i.e., the ethyl ester of the penicilloic acid of penicillin II. The synthesis of this compound may be represented as follows:


(CH3)2C-SH
CHNH2
COOH
+ OHC-CH
NHCOCH2C6H5
COOC2H5
(CH3)2C—S
CH-NH
COOH
CH-CHNHCOCH2C6H5
COOC2H5

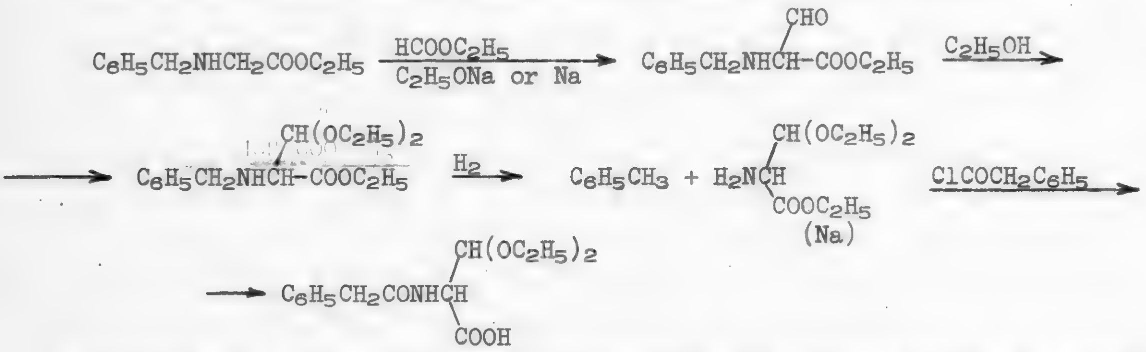
One of the reagents required for the synthesis of penicilloic ester II by the foregoing method is the ethyl ester of α-formylphenaceturic acid, the so-called penaldinic ester II. The preparation of penaldinic ester II by formylating phenaceturic ester in a Claisen reaction was much more difficult for us than preparing the corresponding formyl derivative of hippuric acid (cf Report I [4]), owing to the fact that the phenaceturic ester, in contrast to the hippuric ester, has two reactive methylene groups, and, hence, the formyl group can enter the molecule in different ways. With this in mind, we tried out several variants of synthesizing penaldinic acid II in other ways.

In the first variant, we started out with formylchloroacetic ester, synthesizing its ethyl acetal. We intended to substitute an amino group for the chlorine in the diethyl acetal of formylchloroacetic ester, then condensing the diethyl acetal of formylglycineamide with the acid chloride of phenylacetic acid.


CHO
CHCl
COOC2H5
CH(OC2H5)2
CHCl
COOC2H5
CH(OC2H5)2
CH(NH2)
CONH2
ClCOCH2C6H5
C6H5CH2CONHCH
CH(OC2H5)2
CONH2

We prepared the formylchloroacetic ester by Wislicenus' method [1], employing sodium alcoholate in the reaction. Substituting sodium for potassium lowered the yield of the formylchloroacetic ester much below the yield specified by Wislicenus, viz.: from 70 to 75% down to 18%. Using the dry sodium alcoholate instead of the alcoholic solution (as Wislicenus did) enabled us to increase the yield of the formylchloroacetic ester somewhat (up to 30%). The diethyl acetal of formylchloroacetic ester was secured with good yield by boiling the latter with absolute alcohol and anhydrous HCl. This variant had to be cut short in the amination stage, however. All our attempts to substitute an amino or a benzylamino group for the chlorine in the diethyl acetal of the formylchloroacetic ester met with failure. Nor were we able to replace the chlorine by the more mobile iodine atom.

The second variant may be represented schematically as follows:



$$C_6H_5CH_2NHCH_2COOC_2H_5 \xrightarrow[C_2H_5ONa\ \text{or}\ Na]{HCOOC_2H_5} C_6H_5CH_2NHCH(CHO){-}COOC_2H_5 \xrightarrow{C_2H_5OH}$$

$$\longrightarrow C_6H_5CH_2NHCH(CH(OC_2H_5)_2){-}COOC_2H_5 \xrightarrow{H_2} C_6H_5CH_3 + H_2NCH(CH(OC_2H_5)_2)COOC_2H_5\ (Na) \xrightarrow{ClCOCH_2C_6H_5}$$

$$\longrightarrow C_6H_5CH_2CONHCH(CH(OC_2H_5)_2)COOH$$

Reacting the ethyl ester of N-benzylglycine with ethyl formate and sodium alcoholate or metallic sodium always yielded two individual crystalline substances, no matter what the reaction conditions were, the chemical properties of neither indicating the presence of an oxymethylene or aldehyde group. The structure of these compounds is now under investigation. We have thus been unable to synthesize the ethyl ester of N-benzyl-α-formylglycine.

After our unsuccessful attempts to synthesize penaldinic acid II by the methods outlined above, we made a study of the formylation of phenaceturic acid. After numerous experiments on the formylation of phenaceturic ester under various conditions (using sodium alcoholate, metallic sodium, various temperatures, and various solvents: benzene, ether, and alcohol), we found that the yield of formylphenaceturic ester was highest when phenaceturic ester was reacted with ethylformate and dry sodium alcoholate in absolute ether at room temperature. The resulting formylphenaceturic ester was an oily non-crystallizing substance that consisted of a mixture of the carbonyl and enol forms of formylphenaceturic ester. We identified the formylphenaceturic ester we had synthesized by preparing its dinitrophenylhydrazone.* It is worthy of note that a by-product of the formylation of phenaceturic ester is phenylacetic ester, a rather large am amount of which was recovered. Hence, the formylation of phenaceturic ester is accompanied by a cleavage of the phenaceturic ester and esterification of the phenylacetic acid produced by this cleavage. We established the position of the formyl group in the formylphenaceturic ester as follows: the formyl group was reduced to an alcohol group with aluminum amalgam. The reaction product (its yield being 74% of the theoretical) was cleaved hydrolytically by boiling it with dilute sulfuric acid. This reaction yielded nearly quantitative amounts of serine and phenylacetic acid:

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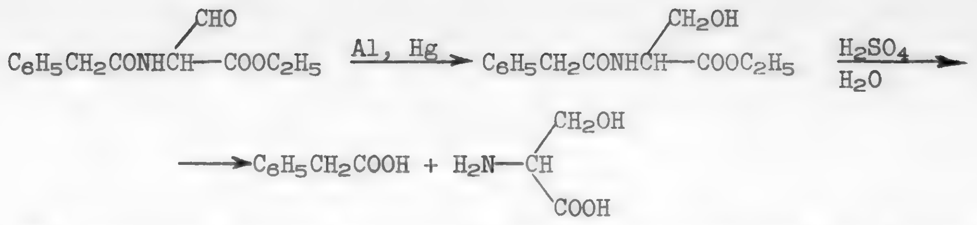
*After we had synthesized formylphenaceturic ester, an abstract was published of an American patent [2], in which ethyl formylphenaceturate was described. The melting point of the dinitrophenylhydrazone of the formylphenaceturic ester we had synthesized was the same as that of the dinitrophenylhydrazone described in this patent.



$$C_6H_5CH_2CONH\overset{CHO}{CH}-COOC_2H_5 \xrightarrow{Al,\ Hg} C_6H_5CH_2CONH\overset{CH_2OH}{CH}-COOC_2H_5 \xrightarrow[H_2O]{H_2SO_4}$$

$$\longrightarrow C_6H_5CH_2COOH + H_2N-\underset{COOH}{\overset{CH_2OH}{CH}}$$

The foregoing equation indicates that phenylacetic acid and serine can be produced only if the formyl group in the formylphenaceturic ester is in the α-position to the esterified carboxyl group.

We thus found that the principal product of the reaction involving the formylation of phenaceturic ester is the ethyl ester of α-formylphenaceturic acid, i.e., penaldic ester II. When α-formylphenaceturic ester was reacted with l-cysteine hydrochloride and a small amount of water at 90°, we secured α-(4-carboxy-2-thiazolidyl)-phenaceturic ester.

The hydrobromide of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic ester was prepared by reacting d,l-dimethylcysteine hydrobromide with α-formylphenaceturic ester at 50-60°.

By analogy with 2-phenyl-4-ethoxymethyleneoxazolinone (cf our preceding report [4]), we synthesized 2-benzyl-4-ethoxymethyleneoxazolinone-(5) by heating the diethyl acetal of α-formylphenaceturic acid with acetic anhydride and pyridine. We were unable to obtain it in crystalline form; we therefore treated the reaction solution with 5% NaOH solution at room temperature as soon as the reaction was over. This saponified the ethoxymethylene group, and we secured crystalline 2-benzyl-4-oxymethyleneoxazolinone-(5) in the free state by acidulating a solution of the Na salt of 2-benzyl-4-oxymethyleneoxazolinone-(5).

The diethyl acetal of α-formylphenaceturic acid was prepared by saponifying the diethyl acetal of α-formylphenaceturic ester with an alcoholic solution of an alkali. The latter was produced in the usual manner from α-formylphenaceturic ester. It is worthy of note that, as in the formylation reaction, the ethyl ester of phenylacetate was found as a by-product of the synthesis of the diethyl acetal of formylphenaceturic ester.

EXPERIMENTAL

Formylchloroacetic ester. 138 g of absolute ethyl alcohol was gradually added to 53.5 g of finely pulverized metallic sodium in 575 ml of absolute ether. When all the alcohol had been added, the reaction mixture was boiled for 2 hours. Then another 420 ml of absolute alcohol was added, and the whole was chilled to -5°. The mixture was stirred while a mixture of 150 g of ethyl formate and 260 g of ethyl chloroacetate was added, the temperature being kept within -5 and -3°. After standing at this temperature for 12 hours the sodium derivative of formylphenaceturic ester was filtered out, washed with ether, desiccated, and dissolved in water. The solution was acidulated with dilute hydrochloric acid. The resulting oil was extracted with ether, and the ether solution was desiccated with anhydrous Na_2SO_4. The ether was driven off, and the residue was distilled at 10 mm residual pressure. A fraction boiling in the 60-85° range was collected. Redistillation yielded crystalline formylchloroacetic ester, which was crystallized from benzene. Its melting point (88-90°) after crystallization from benzene agrees with Wislicenus' figure [1]. The yield was 91.3 g, or 30% of the theoretical.

Diethyl acetal of formylchloroacetic ester. The 91.3 g of formylchloroacetic ester was boiled for 12 hours in 450 ml of absolute alcohol after having been first saturated with 4.5 g of anhydrous HCl. The alcohol was then driven off, and the residue was treated with a K_2CO_3 solution and desiccated with calcined K_2CO_3. After desiccation the acetal was twice distilled in vacuum. The second distillation yielded 89 g of the diethyl acetal of the formylchloroacetic ester, with a b.p. of 101-103° at 7 mm residual pressure.

Found %: Cl 15.7, 15.5. $C_9H_{17}O_4Cl$. Computed %: Cl 15.8.

Ethyl ester of α-formylphenaceturic acid. 7.4 g of absolute ethyl alcohol was gradually added to 2.74 g of pulverized metallic sodium in 40 ml of absolute ether. After all the alcohol had been added, the reaction mixture was boiled for 2 hours, until all the sodium had been converted into sodium alcoholate. After the mixture had cooled, 10 ml of ethyl formate was gradually added, and then 25.4 g of phenaceturic ester was added during the course of 10-15 minutes. The reaction mixture was allowed to stand for 8 days in a hermetically sealed flask, after which it was poured into ice water and repeatedly extracted with ether.* The aqueous solution was acidulated with dilute hydrochloric acid. The oily substance formed during acidulation was extracted with ether. The ether solution was desiccated with anhydrous Na_2SO_4. The ether was driven off; the residue – an oily noncrystallizing substance – was a mixture of the carbonyl and enol forms of the ethyl ester of α-formylphenaceturic acid, totaling 13 g.

Dinitrophenylhydrazone of the ethyl ester of α-formylphenaceturic acid. 0.5 g of the ethyl ester of α-formylphenaceturic acid in 2 ml of ethyl alcohol was mixed with the calculated amount of a saturated aqueous-alcoholic solution of dinitrophenylhydrazine. After a drop of concentrated hydrochloric acid had been added to the solution, the dinitrophenylhydrazone of the α-formylphenaceturic ester began to crystallize out, consisting of yellow needles with a m.p. of 186-187° (after crystallization from alcohol).

4.034 mg substance: 0.572 ml N_2 (22.5°, 741.5 mm). Found %: N 15.98.
$C_{19}H_{19}O_7N_5$. Computed %: N 16.3.

Reduction of the ethyl ester of α-formylphenaceturic acid. Aluminum amalgam was added a little bit at a time to 5 g of the α-formylphenaceturic ester dissolved in 150 ml of ether containing moisture, the rate being such that the hydrogen was slowly evolved all the time. A few drops of water were added to the ether solution from time to time. The reaction was complete within 3 days. The end of the reaction was indicated by the disappearance of coloration with $FeCl_3$ in a sample of the reaction mass. The ester was filtered out of the sludge, desiccated with anhydrous Na_2SO_4, and distilled. The residue, totaling 3.2 g, the ethyl ester of N-phenacetylserine, was an oily substance. Four days of further processing of the sludge with ether yielded another 0.5 g of the ethyl ester of N-phenacetylserine.

Cleavage of the ethyl ester of N-phenacetylserine to phenylacetic acid and serine. 1 g of the ethyl ester of N-phenacetylserine in 40 g of H_2SO_4 (1:15) was boiled until a chilled and filtered sample of the reaction solution yielded no detectable precipitate of phenylacetic acid after reboiling and recooling. When the reaction was over, the solution was cooled. The precipitated phenylacetic acid was filtered out. The phenylacetic acid dissolved in the reaction solution was extracted by repeated processing of the solution with ether. This yielded 0.48 g of phenylacetic acid. An amount of Na_2SO_4 calculated to be enough to neutralize the sulfuric acid was added to the solution. The solution was filtered and evaporated in vacuum to small volume; then it was cooled, and the precipitated serine was filtered out. After alcohol had been added to the mother liquor some more serine was recovered. The serine recovered totaled 0.37 g.

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* The ether solution was desiccated with anhydrous Na_2SO_4. The ether was driven off and the 5.1 g of residue was distilled in vacuum. Almost all the substance distilled at 105-110° and 13 mm residual pressure. Saponification of the resultant product with alcoholic NaOH yielded 4.5 g of phenylacetic acid.

Phenylserine cyanate. 0.3 g of serine (prepared by cleaving the reduced α-formylphenaceturic ester) was dissolved in 3 ml of 1 N NaOH and 1.5 ml of water. The solution was chilled to 0°, and 0.35 g of phenyl isocyanate was added, with vigorous shaking. The small amount of precipitated diphenylurea was filtered out, and the solution was acidulated with dilute hydrochloric acid. Phenylserine cyanate was precipitated. Some more phenylserine cyanate was recovered from the mother liquor by evaporating it. The total yield was 0.55 g. The melting point after crystallization from water (166-167°) agrees with the figure in the literature [3].

3.578 mg substance: 0.407 ml N_2 (24°, 731 mm). 3.712 mg substance: 0.422 ml N_2 (22°, 729 mm). Found %: N 12.56, 12.62.
$C_{10}H_{12}O_4N_2$. Computed %: N 12.49.

Ethyl ester of α-(4-carboxy-2-thiazolidyl)-phenaceturic acid. A mixture of 3 g of the ethyl ester of α-formylphenaceturic acid, 1.9 g of l-cysteine hydrochloride, and 0.5 ml of water was heated over a boiling water bath for 10-15 minutes. The reaction solution was poured into water and neutralized with sodium bicarbonate. The ethyl ester of α-(4-carboxy-2-thiazolidyl)-phenaceturic acid was thrown down as a colorless precipitate totaling 2.8 g. Another 0.5 g of the substance settled out of the mother liquor when it was set aside to stand. After crystallization from 70% alcohol α-(4-carboxy-2-thiazolidyl)-phenaceturic ester was a colorless substance that crystallized in pliant needles with a m.p. of 159-160°.

9.137 mg substance: 5.28 ml 0.01 N H_2SO_4. 8.646 mg substance: 5.03 ml 0.01 N H_2SO_4. Found %: N 8.09, 8.14; S 8.89, 8.97. $C_{16}H_{20}O_5N_2S$ Computed %: N 7.95; S 9.13.

Hydrochloride of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic ester. A mixture of 0.8 g of α-formylphenaceturic ester and 0.5 g of d,l-dimethylcysteine hydrochloride was heated to 60° for 3 hours until the color reaction with sodium nitroprusside that is typical for a thiol group had vanished. When the reaction was complete, the resultant solid was pulverized and crystallized from a mixture of ether and methanol. Crystallization yielded 0.7 g of the hydrochloride of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic ester, a colorless crystalline substance with a m.p. of 181-182°. After the hydrochloride of α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic ester had been boiled with a 5% NaOH solution, the color reaction with sodium nitroprusside reappeared.

7.813 mg substance: 3.79 ml 0.01 N H_2SO_4. Found %: N 6.79.
$C_{18}H_{25}O_5N_2ClS$. Computed %: N 6.72.

Diethylacetal of formylphenaceturic ester. 4 g of α-formylphenaceturic ester in 40 ml of absolute alcohol was boiled for 6 hours after having first been saturated with 0.4 g of anhydrous HCl. The alcohol was driven off in vacuum, the residue was treated with a potash solution, and the acetal extracted with ether. The ether extract was washed with a potash solution and desiccated with anhydrous K_2CO_3. The ether was driven off, and the residue was distilled at 0.8 mm residual pressure. The first low-boiling fraction, totaling 0.6 g, was principally the ethyl ester of phenylacetic acid. The diethyl acetal of α-formylphenaceturic ester (1.5 g) distilled at a b.p. of 170-173° and 0.25 mm.

6.906 mg substance: 0.279 ml N_2 (20.5°, 723 mm). 6.663 mg substance: 18.09 ml $Na_2S_2O_3$. Found %: N 4.47; OC_2H_5 40.75.
$C_{17}H_{25}O_5N$. Computed %: N 4.3; OC_2H_5 41.8.

Diethyl acetal of α-formylphenaceturic acid. 1.35 g of the acetal of α-formylphenaceturic ester was dissolved in a mixture of 0.55 ml of NaOH (sp. gr.

1.457) and 8 ml of alcohol. After standing for 24 hours, the alcohol was driven off in vacuum at a bath temperature of 30-35°. The residue was dissolved in water, treated with charcoal, and filtered, and the filtrate was chilled and then acidulated with HCl (1:2). The oily substance that separated out was extracted with ether; the ether solution was washed with water and desiccated with anhydrous Na_2SO_4. After the ether was driven off, there was left the diethyl acetal of α-formylphenaceturic acid, which crystallized upon standing (0.94 g). The diethyl acetal of α-formylphenaceturic acid, after crystallization from a mixture of benzene and petroleum ether, consisted of colorless needles with a m.p. of 108-109° (with decomposition).

5.905 mg substance: 0.266 ml N_2 (21°, 733.1 mm). 5.897 mg substance: 0.268 ml N_2 (21.5°, 739.0 mm). Found %: N 5.04, 5.12.
$C_{15}H_{21}O_5N$. Computed %: N 4.74.

2-Benzyl-4-oxymethyleneoxazolinone-(5). 0.45 g of the diethyl acetal of α-formylphenaceturic acid was heated in 2.2 ml of acetic anhydride mixed with 0.2 ml of anhydrous pyridine for 20 minutes over a water bath. After the reaction mixture had cooled, it was dissolved in ether and treated repeatedly with 5% alkali (shaking in a separatory funnel at room temperature). The aqueous alkaline solution of the Na salt of 2-benzyl-4-oxymethyleneoxazolinone-(5) was deeply chilled and acidulated with dilute hydrochloric acid. The precipitated crystalline 2-benzyl-4-oxymethyleneoxazolinone-(5) was filtered out, desiccated, and crystallized from CCl_4. The nearly colorless, crystalline 2-benzyl-4-oxymethyleneoxazolinone-(5) fused at 98-100°. It turned blue-green when reacted with $FeCl_3$ in alcoholic solution.

3.675 mg substance: 1.75 ml 0.01 N H_2SO_4. Found %: N 6.67.
$C_{11}H_9O_3N$. Computed %: N 6.89.

SUMMARY

1. A study has been made of the formylation of ethyl phenaceturate, and the optimum conditions have been worked out for the synthesis of α-formylphenaceturic ester. It has been found that the reaction involves the cleavage of the phenaceturic ester as a side reaction and the esterification of the resulting phenylacetic acid.

2. The structure of α-formylphenaceturic acid has been established by reducing the formyl group to an alcohol group and by cleaving the resulting ethyl ester of N-phenacetylserine into phenylacetic acid and serine.

3. Reacting α-formylphenaceturic ester with the hydrochlorides of l-cysteine and d,l-dimethylcysteine yielded the α-(4-carboxy-2-thiazolidyl)- and α-(4-carboxy-5,5-dimethyl-2-thiazolidyl)-phenaceturic esters, respectively.

4. The diethyl acetal of α-formylphenaceturic acid has been synthesized by saponifying the diethyl acetal of α-formylphenaceturic ester with alcoholic alkali.

5. 2-Benzyl-4-ethoxymethyleneoxazolinone-(5) has been synthesized, while saponification of its ethoxymethylene group has yielded 2-benzyl-4-oxymethyleneoxazolinone-(5).

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[2] C.A., 40, 3135 (1946); U.S.Patent 2,294,967.
[3] E.Fischer and H.Leuchs, Ber., 35, 3792.
[4] A.S.Elina and O. Yu.Magidson, J.Gen.Chem. 21, 559 (1951)*

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* See CB translation p. 619 ff.

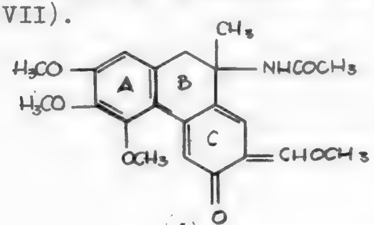
SYNTHETIC RSEARCH ON ANALOGS OF THE ALKALOID COLCHICINE [1]. II.

T. F. Dankova*, T. N. Bokova, N. A. Preobrazhensky

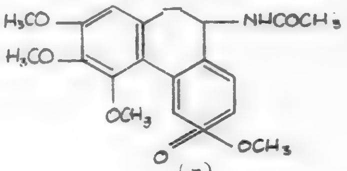
and the Students, A. E. Petrushchenko, I. A. Ilshtein, and N. I. Shvetsov

The formula proposed in 1924 for the alkaloid colchicine (I) [2] has undergone considerable re-examination in recent years, and at the present time we may consider it to be experimentally proven that the rings B and C of colchicine are not six-membered, but rather seven-membered, i.e., colchicine is not a derivative of phenanthrene, but is based on a condensed tricyclic system consisting of one six-membered and two seven-membered rings (II) [3].

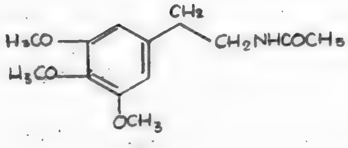
Synthesis of compounds built up on the demonstrated or hypothetical structural elements of the colchicine alkaloid would be of considerable importance in solving the problem of the structure of colchicine and discovering, if possible, substances of simpler structure that exhibit colchicine's action. Some efforts of this sort [4] have shown that derivatives of α- and β-phenylethylamine (III and IV) and derivatives of diphenylmethane (V) are inactive. Derivatives of diphenylpropylamine (VI) possess slight activity. It was concluded that antimitotic activity is inherent in substances that contain the diphenylethylamino group (VII).


CH3
H3CO
NHCOCH3
H3CO
A
B
C
OCH3
CHOCH3
O

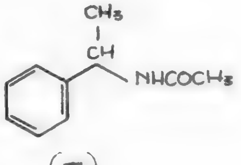
(I)


H3CO
NHCOCH3
H3CO
OCH3
O
OCH3

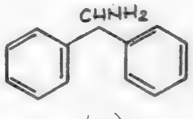
(II)


CH2
H3CO
CH2NHCOCH3
H3CO
OCH3

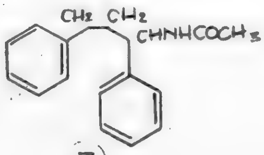
(III)


CH3
CH
NHCOCH3

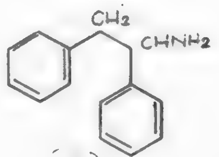
(IV)



(V)


CH2
CH2
CHNHCOCH3

(VI)



(VII)

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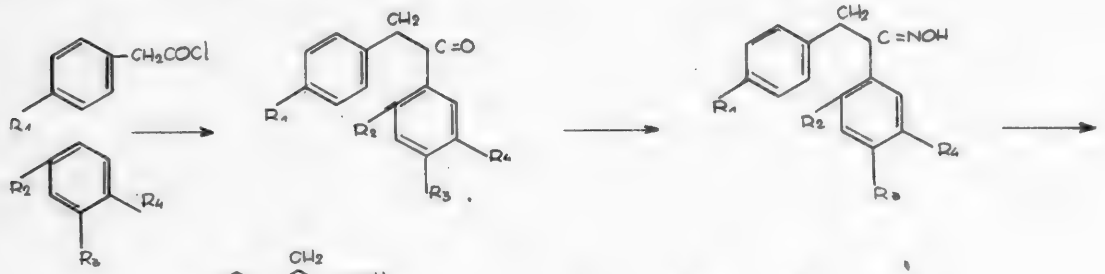
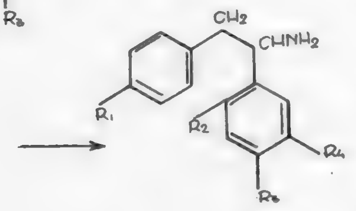
*Deceased.

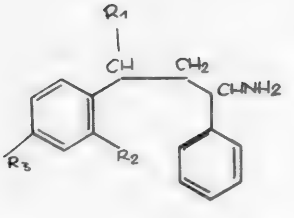
The objective of the present paper has been the synthesis of a series of substances, derivatives of α,β-diphenylethylamine, α,γ-diphenylpropylamine, and β,δ-diphenylbutylamine, the molecules of which contain the structural elements of colchicine with a six- and seven-membered opened ring B. During our syntheses, we also secured a number of unsaturated ketones, the structures of which were close to those of the compounds described above. These substances may likewise be of interest for physiological tests, since there are data showing that many aromatic ketones are powerful protoplasm poisons [5].

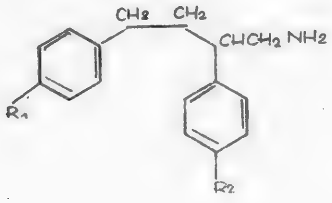
The α,β-diphenylethylamine and its derivatives (VIII, IX, X, XI, XII) were synthesized by a Friedel-Crafts reaction: condensing the acid chloride of phenylacetic acid with benzene and its substituted compounds, resulting in derivatives of β-keto-α,β-(diphenyl)-ethane. Reduction of the oximes of these ketones yielded the corresponding amines.





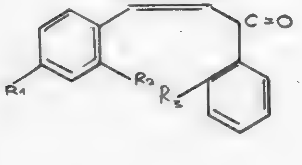
	R_1	R_2	R_3	R_4
(VIII)	H	H	H	H
(IX)	H	H	OH	H
(X)	H	H	OCH_3	H
(XI)	H	OCH_3	H	OCH_3
(XII)	OCH_3	H	OCH_3	H





	R_1	R_2	R_3
(XIII)	H	Cl	H
(XIV)	NH_2	H	OCH_3

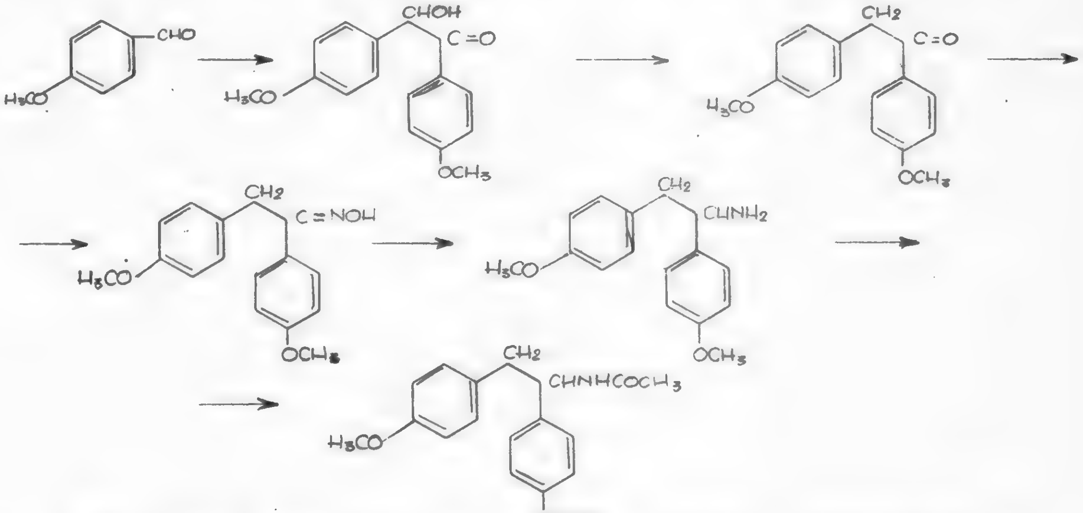
	R_1	R_2
(XV)	OCH_3	H
(XVI)	OCH_3	OCH_3



	R_1	R_2	R_3
(XVII)	H	NO_2	H
(XVIII)	H	NH_2	H
(XIX)	H	H	NO_2
(XX)	H	H	NH_2
(XXI)	OCH_3	H	NO_2
(XXII)	OCH_3	H	NH_2
(XXIII)	OCH_3	H	H

The ketone was subjected to the action of anhydrous ammonium formate at high temperature to produce α,β-(diphenyl)-ethylamine [6]. The acid chloride of phenylacetic acid required for the reaction was prepared by saponifying phenylacetonitrile and reacting the resulting acid with phosphorus trichloride. The condensation was performed in benzene, carbon disulfide, or nitrobenzene at room temperature or by heating to from 40 to 80°. The oximes, prepared by the action of hydroxylamine hydrochloride in alcoholic solution with sodium carbonate, were reduced to the amines by the action of sodium amalgam in alcoholic solution with acetic acid.

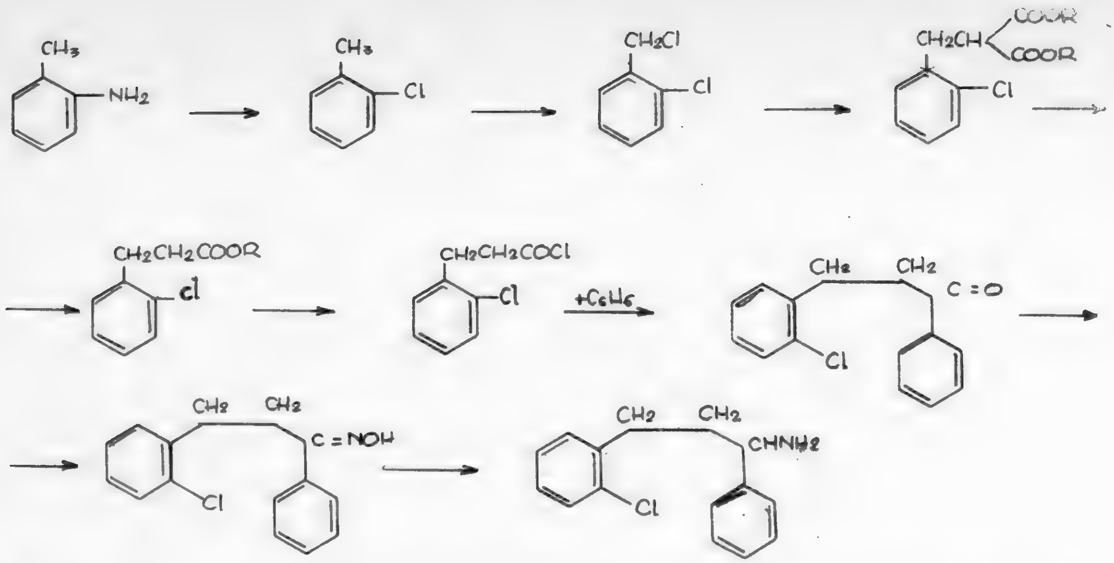
α,β-Di-(4-methoxyphenyl)-ethylamine (XII) was synthesized via anisoin by condensing anisaldehyde in the presence of potassium cyanide [7]. The anisoin was converted into desoxyanisoin by reacting it with stannous chloride and hydrochloric acid. The oxime, prepared in a reaction with hydroxylamine hydrochloride [8], was reduced to the amine by sodium amalgam. The acetyl derivative of the amine was prepared by reacting a base of the amine with acetic anhydride and water.



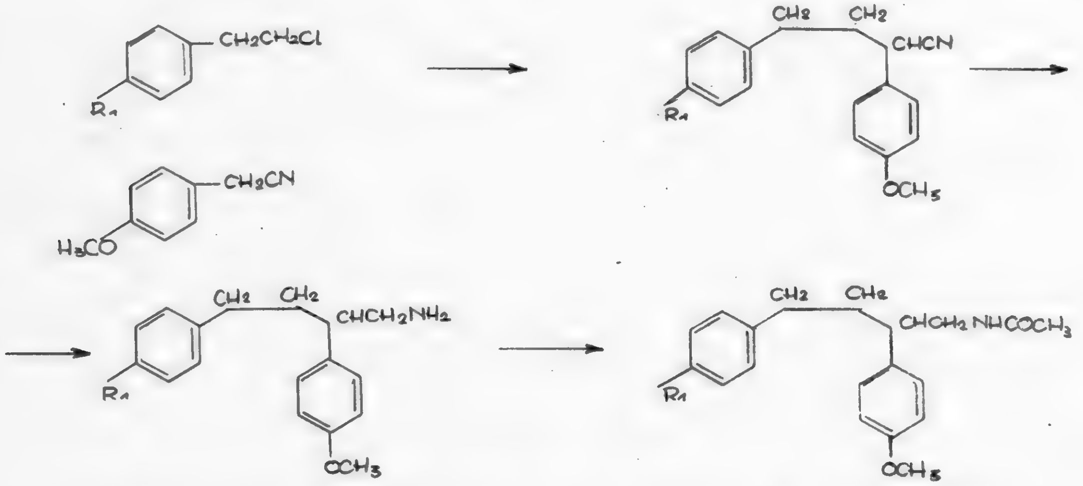
Derivatives of α-γ-diphenylpropylamine. α-(Phenyl)-γ-(2-chlorophenyl)-propylamine (XIII) was prepared in a Friedel-Crafts reaction from the acid chloride of 2-chlorophenylpropionic acid and benzene, followed by reduction of the oxime secured from the γ-keto-γ-phenyl-α-(2-chlorophenyl)-propane formed during the condensation (cf. Page 870).

The acid chloride of 2-chlorophenylpropionic acid was prepared from o-toluidine, which was converted into o-chlorotoluene by a Sandmeyer reaction, the latter in turn being converted into o-chlorobenzyl chloride by chlorination with pentachloride and illumination by a 100-watt electric light bulb. The condensation of the latter compound with sodium malonic ester in the presence of sodium ethylate yielded o-chlorobenzyl malonate together with α,β-2,2'-dichlorodiphenylethane, which was evidently synthesized under these conditions by the condensation of two molecules of o-chlorobenzyl chloride. Saponification of the ester yielded 2-chlorophenylpropionic acid, which was converted into the acid chloride by phosphorus pentachloride.

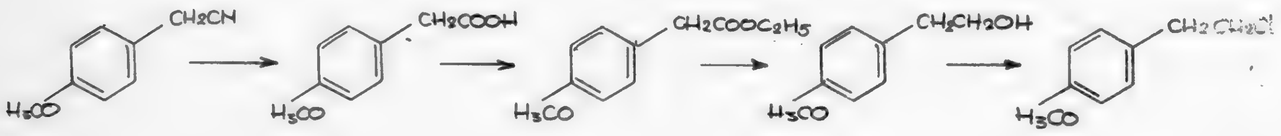
α-(Phenyl)-γ-(4-methoxyphenyl)-γ-(amino)-propylamine (XIV) was synthesized by heating γ-keto-γ-phenyl-α-(4-methoxyphenyl)-propylamine (XXII) with anhydrous ammonium formate to 220-230° in an ampoule. Its formation involved the addition of ammonia in addition to the conversion of the keto group into an amino group.


CH3
NH2
CH3
Cl
CH2Cl
Cl
CH2CH
COOR
COOR
Cl
CH2CH2COOR
Cl
CH2CH2COCl
Cl
+C6H6
CH2
CH2
C=O
Cl
CH2
CH2
C=NOH
Cl
CH2
CH2
CHNH2
Cl

The derivatives of β,δ-diphenylbutylamine; β,δ-di-(4-methoxyphenyl)-butylamine (XVI) and β-(methoxyphenyl)-δ-(phenyl)-butylamine (XV), were synthesized by condensing α-chloro-β-(4-methoxyphenyl)-ethane and α-chloro-β-phenylethane with 4-methoxyphenylacetonitrile in anhydrous toluene with sodamide. The resultant diphenyl derivatives of butyronitrile were hydrogenated with Raney's nickel to the respective amines, which were then acetylated to their acetyl derivatives:

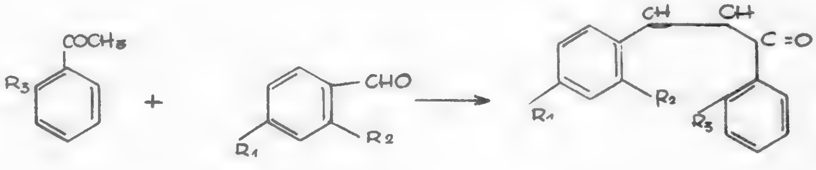

CH2CH2Cl
R1
CH2CN
H3CO
CH2
CH2
CHCN
R1
OCH3
CH2
CH2
CHCH2NH2
R1
OCH3
CH2
CH2
CHCH2NHCOCH3
R1
OCH3

α-Chloro-β-(4-methoxyphenyl)-ethane was prepared from 4-methoxyphenylacetonitrile by saponifying the latter to 4-methoxyphenylacetic acid, the ethyl ester of which was reduced with metallic sodium in alcohol to yield 4-methoxyphenylethyl alcohol. The latter was converted into α-chloro-β-(4-methoxyphenyl)-ethane by treating it with phosphorus pentachloride in anhydrous benzene:


CH2CN
H3CO
CH2COOH
H3CO
CH2COOC2H5
H3CO
CH2CH2OH
H3CO
CH2CH2Cl
H3CO

α-Chloro-β-phenylethane was prepared similarly from the β-phenylethyl alcohol and phosphorus pentachloride.

The derivatives of γ-keto-α,γ-diphenylpropylene were synthesized by condensing benzaldehyde and its derivatives with acetophenone and substituted acetophenones:



γ-Keto-γ-(phenyl)-α-(4-methoxyphenyl)-propylene (XXIII) and γ-keto-γ-(phenyl)-α-(2-nitrophenyl)-propylene (XVII) were synthesized by condensing acetophenone with 4-methoxybenzaldehyde and 2-nitrobenzaldehyde, respectively. The latter was prepared by oxidizing 2-nitrotoluene with chromic oxide in acetic acid and acetic anhydride [9].

The reaction of benzaldehyde and 2-methoxybenzaldehyde with 2-nitroacetophenone, prepared by condensing the acid chloride of 2-nitrobenzoic acid with acetoacetic ester [10], yielded γ-keto-γ-(2-nitrophenyl)-α-(phenyl)-propylene (XIX) and γ-keto-γ-(2-nitrophenyl)-α-(4-methoxyphenyl)-propylene (XXI), respectively. Reduction of the resulting nitro ketones with tin and hydrochloric acid or, even better, with activated iron in benzene [11] yielded the corresponding amines: γ-keto-γ-phenyl-α-(2-aminophenyl)-propylene (XVIII); γ-keto-γ-(2-aminophenyl)-α-(phenyl)-propylene (XX); and γ-keto-γ-(2-aminophenyl)-α-(4-methoxyphenyl)-propylene (XXII), which served as the initial materials for our research on the synthesis of the tricyclic compounds.

EXPERIMENTAL

α,β-Diphenylethylamine hydrochloride (VIII). The acid chloride of phenylacetic acid was prepared by reacting 36 g of phosphorus trichloride with 40 g of phenylacetic acid dissolved in 80 ml of absolute benzene and then boiling the reaction mass for 3.5 hours. After the solvent had been driven out of the benzene solution, the residue was distilled in vacuum, yielding 27 g (59% of the theoretical) of the acid chloride of phenylacetic acid with a b.p. of 95-95.5° at 14 mm.

Desoxybenzoin was synthesized by reacting a solution of 5 g of the acid chloride of phenylacetic acid in 25 ml of absolute benzene with 8.5 g of aluminum trichloride at room temperature [12]. This yielded 5.4 g of desoxybenzoin as slightly yellowish crystals with a m.p. of 54-55°. Yield: 28%.

The hydrochloride of α,β-diphenylethylamine was synthesized by heating 1.5 g of desoxybenzoin and 3 g of anhydrous ammonium formate for 4-5 hours to 220-230° in a metal ampoule, and then boiling the solid reaction mass with 15 ml of a 20% alcoholic solution of potassium hydroxide. The reaction product was distilled with steam, and the distillate was acidulated with hydrochloric acid and evaporated until it began to crystallize. The resultant α,β-diphenylethylamine hydrochloride had a m.p. of 247-248° after recrystallization from alcohol. Yield: 1 g (56.5% of the theoretical).

4.57 mg substance: 0.24 ml N_2 (22°, 740 mm). Found %: N 5.83.
$C_{14}H_{15}N \cdot HCl$. Computed %: N 5.99.

α-(4-Hydroxyphenyl)-β-phenylethylamine (IX). 18.5 g of aluminum trichloride was added a little bit at a time, with vigorous stirring, to a solution of 10 g of the acid chloride of phenylacetic acid and 6.1 g of phenol in 30 g of nitrobenzene, heated to 80°. Heating was then continued for another 15 minutes, the mixture was cooled to 30°, the dark-red, syrupy reaction product was poured into 150 ml of water acidulated with a few drops of concentrated hydrochloric acid, and the mixture was cautiously heated for a few minutes. The reaction product that precipitated upon cooling was filtered out, washed with water, and recrystallized from dilute alcohol. This yielded 5 g of β-keto-α-phenyl-β-(4-hydroxyphenyl)-ethane, with a m.p. of 141-142°. Yield: 32.6% of the theoretical.

Synthesis of the oxime of β-keto-α-phenyl-β-(4-hydroxyphenyl)-ethane: 1.2 g of hydroxylamine hydrochloride and 1 g of sodium carbonate were dissolved in 10 ml of water and added to 3.5 g of β-keto-α-phenyl-β-(4-hydroxyphenyl)-ethane dissolved in 80 ml of alcohol, and the mixture was boiled for 6 hours. Then the same amounts of hydroxylamine hydrochloride (1.2 g) and sodium carbonate (1 g) were added, and boiling was continued for another 6 hours. The solvent was driven off, and the residual oil cyrstallized upon standing. It was dissolved in a small quantity of alcohol and poured into a large quantity of water. Yield of the oxime: 2.9 g (78% of the theoretical), with a m.p. of 85-86°.

135 g of 3.5% sodium amalgam was gradually added, with constant stirring, to a solution of 2.9 g of the oxime in 29 ml of alcohol acidulated with glacial acetic acid, heated to 60°, care being taken to keep the mixture acid. When the reaction was complete, 29 ml of water was added to the hot solution, which was allowed to cool; then another 29 ml of water was added, and the mass was allowed to stand for 12 hours until all the unreacted oxime had settled out. The filtered solution was treated with concentrated ammonia until its reaction was alkaline, and the resultant precipitate was desiccated and then recrystallized from a benzene-ligroin mixture. This yielded α-(4-hydroxyphenyl)-β-phenylethylamine as colorless crystals that are freely soluble in alcohol and benzene and slightly soluble in ether and ligroin. M.p. 106-107°. Yield: 1.8 g (67% of the theoretical).

The hydrochloride of the amine, prepared by reacting an alcoholic solution of the base with an ethereal solution of hydrogen chloride, consisted of thin, colorless crystals with a m.p. of 245-246° after recrystallization from an alcohol-ether mixture. They were freely soluble in water and alcohol, though insoluble in ether.

5.25 mg substance: 0.26 ml N_2 (20°, 753 mm). Found %: N 5.65.
$C_{14}H_{15}ON \cdot HCl$. Computed %: N 5.62.

α-(4-Methoxyphenyl)-β-phenylethylamine (X). β-Keto-α-phenyl-β-(4-methoxyphenyl)-ethane was prepared from 1.9 g of anisole and 2.4 g of the acid chloride of phenylacetic acid in 12 g of carbon disulfide by adding aluminum chloride to the mixture at room temperature and then heating the mixture for an hour over a water bath [13]. The yield of β-keto-α-phenyl-β-(4-methoxyphenyl)-ethane, with a m.p. of 74-75° after recrystallization from alcohol, was 1.2 g (31% of the theoretical.

The oxime of β-keto-α-phenyl-β-(4-methoxyphenyl)-ethane was synthesized by method described above, by twice adding a solution of 0.3 g of hydroxylamine hydrochloride and 0.2 g of sodium carbonate in 4 ml of water to 1 g of β-keto-α-phenyl-β-(4-methoxyphenyl)-ethane. The m.p. of the oxime was 109-110° after recrystallization from 80% alcohol. Yield: 0.72 g (60% of the theoretical).

α-(4-Methoxyphenyl)-β-phenylethylamine was synthesized by reducing 0.5 g of the oxime in 5 ml of alcohol with 23 g of 3.5% sodium amalgam, the reaction mixture being acidulated with glacial acetic acid and heated to 60°. The reaction product was recovered and purified as described for the amine (IX). α-(4-Methoxyphenyl)-β-phenylethylamine was recovered as a thick oil that could not be distilled without decomposition; it yielded yellowish crystalline needles of the hydrochloride when reacted with an ethereal solution of hydrogen chloride, and fused at 196-197° after double recrystallization from an alcohol-ether mixture. Yield: 0.4 g (76% of the theoretical).

5.0 mg substance: 0.24 ml N_2 (25°, 755 mm). Found %: N 5.33. $C_{15}H_{17}NO \cdot HCl$. computed %: N 5.56.

α-(2,5-Dimethoxyphenyl)-β-phenylethylamine. β-Keto-α-phenyl-β-(2,5-dimethoxyphenyl)-ethane was synthesized by reacting 3 g of the acid chloride of phenylacetic acid with 2.7 g of 2,5-dimethoxybenzene in 15 ml of carbon disulfide while 4.5 g of aluminum trichloride was gradually added, with vigorous stirring, at room temperature, after which the reaction mass was heated over a water bath for 2.5-3 hours. The mixture was cooled, 20 ml of ice water and 2 ml of hydrochloric acid were added, the carbon disulfide and the unreacted 2,5-dimethoxybenzene were driven off with steam. The residue was chilled, separated from the aqueous layer, and treated with a 4% potassium hydroxide solution. The thick dark-yellow oil crystallized into a solid mass. Recrystallization from alcohol yielded 2 g of β-keto-α-phenyl-β-(2,5-dimethoxyphenyl)-ethane, with a m.p. of 46-48°. Yield: 40% of the theoretical.

The reaction of 1.9 g of β-keto-α-phenyl-β-(2,5-dimethoxyphenyl)-ethane dissolved in alcohol with 0.54 g of hydroxylamine hydrochloride and 0.43 g of sodium carbonate yielded an oily oxime that crystallized upon standing. The oxime of β-keto-α-phenyl-β-(2,5-dimethoxyphenyl)-ethane, which was purified by pouring a concentrated alcoholic solution into a large quantity of water, had a m.p. of 85-87°. The yield was 1.6 g (80% of the theoretical).

6.6 mg substance: 0.31 ml N_2 (19°, 754 mm). Found %: N 5.34.
$C_{16}H_{17}O_3N$. Computed %: N 5.17.

1 g of the oxime was reduced in alcoholic solution with 44 g of 3.5% sodium amalgam to which 8.4 ml of glacial acetic acid had been added. This yielded 0.8 g of the amine base as a very thick, yellowish oil that formed a hydrochloride when reacted with an ethereal solution of hydrogen chloride: recrystallization from an alcohol-ether mixture yielded the yellowish crystals of the hydrochloride, with a m.p. of 161-162°. Yield: 85% of the theoretical.

4.055 mg substance: 0.17 ml N_2 (25°, 746 mm). Found %: N 4.60.
$C_{16}H_{19}O_2N \cdot HCl$. Computed %: N 4.77.

α,β-Di-(4-methoxyphenyl)-ethylamine (XII). Anisoin was synthesized by a benzoin condensation of 15 g of anisaldehyde in 20 ml of alcohol under the influence of 3 g of potassium cyanide dissolved in 12 ml of water [7]. The melting point of the resultant anisoin was 107-109°

Desoxyanisoin was synthesized by reducing a solution of 2 g of anisoin in 8 ml of alcohol by heating it over a water bath with 1.8 g of tin and 3 ml of concentrated hydrochloric acid and adding a minute crystal of copper sulfate [8]. The yield of desoxyanisoin was 1.6 g (95% of the theoretical); m.p. 108-109°.

The oxime of desoxyanisoin was prepared by reacting 1.6 g of desoxyanisoin dissolved in 5 ml of pyridine with 0.46 g of hydroxylamine hydrochloride – boiling the reaction mixture for 3 hours over a water bath and adding 16 ml of water. The yield of the oxime, with a m.p. of 118-120°, was 1.6 g (94% of the theoretical).

α,β-Di-(4-methoxyphenyl)-ethylamine was synthesized by reducing an alcoholic solution of 1.6 g of the oxime with 70 g of 3.5% sodium amalgam to which 13 ml of glacial acetic acid had been added. The amine yield was 1.3 g of colorless crystals, with a m.p. of 97-98° after recrystallization from alcohol. The base was readily soluble in hot alcohol, slightly soluble in ether, and insoluble in water.

4.90 mg substance: 0.25 ml N_2 (24°, 743 mm). Found %: N 5.40.
$C_{16}H_{19}O_2N$. Computed %: N 5.44.

The hydrochloride of α,β-di-(4-methoxyphenyl)-ethylamine, prepared in the usual manner, consisted of thin colorless crystals with a m.p. of 203-204° after recrystallization from an absolute alcohol-ether mixture, which were freely soluble in alcohol and hot water and insoluble in ether.

5.00 mg substance: 0.22 ml N_2 (22°, 754 mm). Found %: N 4.94.
$C_{16}H_{19}O_2N \cdot HCl$. Computed %: N 4.77.

α,β-Di-(4-methoxyphenyl)-ethylacetamine was synthesized by reacting the amine base (XII) with a tenfold excess of acetic anhydride in ice water, the mixture being vigorously agitated and chilled with ice. The crystals that formed were filtered out, washed with water, and recrystallized from a benzene-ligroin mixture; m.p. 151-152°; soluble in alcohol and benzene; insoluble in ligroin.

4.49 mg substance: 0.20 ml N_2 (24°, 755 mm). Found %: N 4.94.
$C_{18}H_{21}O_3N$. Computed %: N 4.68.

α-Phenyl-γ-(2-chlorophenyl)-propylamine. o-Chlorobenzyl chloride was synthesized by exposing a boiling mixture of 30 g of o-chlorotoluene, prepared by a Sandmeyer reaction [14], and 1 g of phosphorus pentachloride to anhydrous chlorine and the light from 100-watt lamp until the temperature of the mixture's vapor reached 208-210°. Vacuum fractionation of the reaction product yielded 30 g of o-chlorobenzyl chloride, with a m.p. of 86-90° at 8 mm [15]. Yield: 78% of the theoretical.

38 g of diethyl malonate was added gradually, with constant stirring, to sodium alcoholate, prepared with 5.7 g of sodium and 118 ml of absolute alcohol, and 36 g of o-chlorobenzyl chloride was added after the mixture had been stirred for 20 minutes. The reaction mass was heated for 3 hours over a water bath, the alcohol was driven off in vacuum, and the residue was decomposed with water and extracted with chloroform. The solvent was then driven off, and the residue distilled in vacuum. The diethyl ester of o-chlorobenzylmalonic acid was secured as a thick, colorless liquid, which was readily soluble in all organic solvents, though insoluble in water, and had a b.p. of 175-176° at 6 mm. The yield was 36 g, (62% of the theoretical).

d_{15}^{15} 1.187; n_D^{15} 1.5039; MR_D 71.4; computed 71.2.

The residue in the distilling flask crystallized into a solid crystalline mass. Repeated recrystallization from alcohol yielded colorless crystals of α,β-2,2'-dichlorodiphenylethane, with a b.p. of 250° at 6 mm and a m.p. of 65°.

o-Chlorophenylpropionic acid was synthesized from 38 g of the diethyl ester of o-chlorobenzylmalonic acid by saponifying the latter by boiling it with 200 ml of concentrated hydrochloric acid and 100 ml of water for 13 hours. The crystals that settled out when the reaction mixture cooled were dissolved in 10% sodium hydroxide, the solution was washed with chloroform, and the acid was recovered by adding hydrochloric acid. o-Chlorophenylpropionic acid consisted of minute colorless crystals; its melting point was 91-93° after recrystallization from ligroin. Its yield was 16 g (72% of the theoretical).

Acid chloride of o-chlorophenylpropionic acid. This was prepared by reacting 10 g of chlorophenylpropionic acid with 11 g of phosphorus pentachloride, and heating the mixture to 140-160° for 4 hours after the violent reaction had subsided. Distillation of the reaction mass in vacuum yielded the acid chloride as a highly mobile, colorless mass with a b.p. of 130-133° at 10 mm, which turned dark rapidly when exposed to the air. Yield: 7.5 g (70% of the theoretical).

d_{15}^{15} 1.278; n_D^{15} 1.546. MR_D 50.195; computed 49.906.

Five grams of the acid chloride of *o*-chlorophenylpropionic acid was dissolved in 40 ml of absolute benzene and treated for an hour with 10 g of aluminum trichloride added in small batches, with constant stirring, after which the reaction mass was set aside to stand overnight. The next day it was decomposed with water and extracted with ether. The extract was washed with alkali and with water until its reaction was neutral, the ether was driven off, and the residue was distilled in vacuum. γ-Keto-γ-phenyl-α-(2-chlorophenyl)-propane distilled at 200-205° and 12 mm as a light-yellow oil, which slowly crystallized when left for a long time in a vacuum desiccator. Double recrystallization from alcohol yielded colorless crystals with a m.p. of 39-40°, which were freely soluble in ether, benzene, and hot 75% alcohol, but were insoluble in water. Yield: 1.3 g (21.5% of the theoretical).

The oxime of γ-keto-γ-phenyl-α-(2-chlorophenyl)-propane was synthesized by twice adding 0.3 g of hydroxylamine hydrochloride and 1.8 g of sodium carbonate in 4 ml of water to 1 g of γ-keto-γ-phenyl-α-(2-chlorophenyl)-propane dissolved in 24 ml of alcohol. The mixture was heated for 10 hours over a water bath, the alcohol was driven off, and the oxime settled out as a light-yellow oil that crystallized. After recrystallization from dilute alcohol, the oxime of γ-keto-γ-phenyl-α-(2-chlorophenyl)-propane consisted of colorless crystals with a m.p. of 103-104°. Yield: 0.54 g (51% of the theoretical).

5.93 mg substance: 0.28 ml N_2 (22°, 754 mm). Found %: N 5.32.
$C_{15}H_{14}ONCl$. Computed %: N 5.39.

α-Phenyl-γ-(2-chlorophenyl)-propylamine was prepared by reducing 0.5 g of the oxime in 6 ml of alcohol at 40-60° with 22 g of 3.5% sodium amalgam to which 7 ml of glacial acetic acid had been added. Alkalinizing the reaction solution with ammonia yielded the base of the synthesized amine as a thick viscous oil that could not be distilled in vacuum without decomposition. Reacting an alcoholic solution of the base with an ethereal solution of hydrogen chloride yielded the crystalline hydrochloride of α-phenyl-γ-(2-chlorophenyl)-propylamine, which had a m.p. of 200-200.5° after recrystallization from an alcohol-ether mixture. Yield: 0.3 g (55% of the theoretical).

4.26 mg substance: 0.192 ml N_2 (22°, 744.5 mm). Found %: N 5.00.
$C_{15}H_{16}NCl \cdot HCl$. Computed %: N 4.96.

β,γ-Di-(4-methoxyphenyl)-butylamine (XVI). 44 g of 4-methoxyphenylacetonitrile, prepared by a method we had developed previously [1], and 74 g of a 30% solution of sodium hydroxide were heated to 100-110° for 10 hours over an oil bath, with constant stirring; the 53 ml of water was added, and the heating and stirring were continued until no more ammonia was evolved. The unreacted nitrile was extracted from the reaction mass with benzene, and the mass was acidulated with dilute sulfuric acid. The precipitated 4-methoxyphenylacetic acid has a m.p. of 84-86° after desiccation. Yield: 88-89%.

The ethyl ester of 4-methoxyphenylacetic acid was prepared in the usual manner, by esterifying 24.6 g of the acid in 74 g of ethyl alcohol by boiling it with 1.4 g of concentrated sulfuric acid with constant stirring for 7 hours. After the alcohol had been driven off, the resultant ester was recovered by pouring the reaction mass into water, separating the resultant oil, washing it with a weak solution of soda and with water, desiccating it in an ether solution above sodium sulfate; then the solvent was driven off, and the residue was distilled in vacuum. The yield of the ethyl ester of 4-methoxyphenylacetic acid, with a b.p. of 139-141° at 7 mm, was 20.7 g (76% of the theoretical).

4-Methoxyphenylethyl alcohol was synthesized by reducing 17.5 g of the ethyl ester of 4-methoxyphenylacetic acid with 12.8 g of sodium in 71 ml of absolute alcohol. The yield was 6.7 g (54.5%); b.p. 145-147° at 7 mm.

α-Chloro-β-(4-methoxyphenyl)-ethane was synthesized by reacting 7.4 g of 4-methoxyphenylethyl alcohol dissolved in 15 ml of anhydrous benzene with a mixture of 10.4 g of phosphorus pentachloride and 15 ml of anhydrous benzene [16]. The solvent was driven off, and the residue was distilled in vacuum. This yielded 5 g of α-chloro-β-(4-methoxyphenyl)-ethane (60% of the theoretical), with a b.p. of 102-103° at 7 mm.

1.1 g of sodamide was gradually added, with constant stirring, to 4 g of α-chloro-β-(4-methoxyphenyl)-ethane and 3.8 g of 4-methoxyphenylacetonitrile, dissolved in 20 g of anhydrous toluene, so as to keep the temperature from rising higher than 30-40°; the mixture was then gradually heated to boiling and boiled for 1 hour with constant stirring. 60 ml of water was added to the reaction mass after it had cooled, the toluene layer was separated, the aqueous solution was twice extracted with small quantities of toluene, and the combined extracts were desiccated above sodium sulfate. The solvent was driven off, and the residual thick oil was treated with alcohol, yielding a crystalline product with a m.p. of 71-74° that was insoluble in water or cold alcohol, sparingly soluble in ether, and freely soluble in hot alcohol. Double recrystallization from alcohol yielded the colorless lamellar crystals of α,γ-di-(4-methoxyphenyl)-butyronitrile, with a m.p. of 73-74°. Yield: 2.15 g (43% of the theoretical).

4.575 mg substance: 0.21 ml N_2 (18°, 746 mm). Found %: N 5.25.
$C_{18}H_{19}O_2N$. Computed %: N 4.98.

β,δ-Di-(4-methoxyphenyl)-butylamine was synthesized by hydrogenating 1 g of the nitrile dissolved in 60 ml of alcohol with 1 g of Raney's nickel at a pressure of 1.8 atm for 10 hours at a temperature of 50-60° with effective stirring. The hydrogen absorbed was 87% of the calculated amount. The catalyst was filtered out of the reaction mass, the alcohol was driven off, the residue was treated with ether to eliminate the unreacted nitrile, and the base was recovered by adding potash. After the extracts had been desiccated over sodium sulfate, the ether was driven off; the residue consisted of β,δ-di-(4-methoxyphenyl)-butylamine, a very thick, viscous yellow oil, which crystallized slowly when left to stand for a long time in a vacuum desiccator. It is insoluble in water, and freely soluble in ether and hot alcohol. Yield: 0.4 g (40% of the theoretical).

0.0541 g substance: 0.1498 g CO_2; 0.0385 g H_2O. 5.1 mg substance:
0.225 ml N_2 (25°, 746.5 mm). Found %: C 75.51; H 7.91;
$C_{18}H_{23}O_2N$. Computed %: C 75.79; H 8.07; N 4.91.

Heating 0.3 g of the amine (XVI) with 1 g of acetic anhydride over a water bath for 1.5 hours and driving off the excess acetic anhydride and acetic acid in vacuum yielded a thick yellow oil; after it had been washed with water and dissolved in ether, the ether solution desiccated above sodium sulfate, and the solvent driven off, it could not be distilled in a 4-mm vacuum without decomposing. Analysis indicated that it was the diacetyl derivative of the amine.

0.265 mg substance: 0.225 ml N_2 (25°, 745 mm). Found %: N 3.93.
$C_{22}H_{27}O_4N$. Computed %: N 3.80.

The monoacetyl derivative – β,δ-di-(4-methoxyphenyl)-acetamine – was synthesized by treating the diacetyl derivative with 10 ml of an alcoholic solution of potassium hydroxide for 5 hours over a boiling water bath. The oil recovered after the solvent had been driven off was purified by boiling it with petroleum ether. Freely soluble in ether and alcohol, insoluble in petroleum ether, decomposes when distilled at 4 mm.

5.02 mg substance: 0.19 ml N_2 (25°, 753.5 mm). 0.2860 g substance: 1.8 ml 0.5 N KOH. Found %: N 4.19; CH_3CO 13.54 (Perkin).
$C_{20}H_{25}O_3N$. Computed %: N 4.25; CH_3CO 13.15.

β-(4-Methoxyphenyl)-δ-phenylbutylamine (XV). α-Chloro-β-phenylethane was prepared from 7.6 g of phenylethyl alcohol dissolved in 15 ml of anhydrous benzene and a mixture of 10.4 g of phosphorus pentachloride and 15 ml of anhydrous benzene. The yield of α-chloro-β-phenylethane was 6.5 g (74.5% of the theoretical); b.p. 91-93° at 20 mm.

α-(4-Methoxyphenyl)-γ-(phenyl)-butyronitrile was synthesized by condensing 6.5 g of α-chloro-β-phenylethane with 7.8 g of 4-methoxyphenylacetonitrile in 35 g of anhydrous toluene to which 1.8 g of sodamide had been added, as described in the synthesis of the nitrile of α,γ-di-(4-methoxyphenyl)-butyronitrile. This yielded 2.7 g (23.3% of the theoretical) of α-(4-methoxyphenyl)-γ-(phenyl)-butyronitrile, a syrupy mass that was freely soluble in ether and alcohol, but insoluble in water.

4.6 mg substance: 0.24 ml N_2 (25°, 745.5 mm). Found %: N 5.71.
$C_{17}H_{17}ON$. Computed %: N 5.57.

2.7 g of the nitrile was hydrogenated in 100 ml of alcohol at a pressure of 1.8 atm with Raney's nickel for 11 hours at 60-65° with constant stirring, 75% of the calculated quantity of hydrogen being absorbed. The reaction product was isolated as described in the synthesis of the amine (XVI). This yielded 0.8 g (30% of the theoretical) of β-(4-methoxyphenyl)-δ-phenylbutylamine, a thick, syrupy oil that was insoluble in water, though soluble in organic solvents.

6 mg substance: 0.305 ml N_2 (25°, 746 mm). Found %: N 5.66.
$C_{17}H_{21}ON$. Computed %: N 5.49.

β-(4-Methoxyphenyl)-δ-phenylbutylacetamine. Acetylation of 0.7 g of the amine (XV) with 2 ml of acetic anhydride yielded 0.6 g of a thick, yellow, syrupy oil that was freely soluble in alcohol, ether, benzene, and acetone, slightly soluble in petroleum ether, and insoluble in water.

6.4 mg substance: 0.285 ml N_2 (24°, 750 mm). 0.2024 g substance: 1.41 ml 0.5 N KOH. Found %: N 4.91; CH_3CO 14.97 (Perkin).
$C_{19}H_{28}O_2N$. Computed %: N 4.72; CH_3CO 14.47.

γ-Keto-γ-phenyl-α-(4-methoxyphenyl)-propylene (XXIII). A solution of sodium methylate, prepared from 0.38 g of sodium and 3.5 ml of absolute methanol, was gradually added, with chilling and constant stirring, to a mixture of 5 g of 4 methoxybenzaldehyde dissolved in 20 ml of absolute alcohol and 5 ml of acetophenone dissolved in 20 ml of absolute alcohol. The reaction mass was allowed to stand in a cold place for 24-25 hours. The resultant precipitate was filtered out and washed with absolute ether. Recrystallization from alcohol yielded light-yellow crystals with a m.p. of 75-75.5°. The yield was 5 g (57% of the theoretical).

α-Phenyl-γ-(4-methoxyphenyl)-γ-(amino)-propylamine (XXIV). 1 g of γ-keto-γ-phenyl-α-(4-methoxyphenyl)-propylene (XXIII) was heated in a metallic ampoule to 220-230° for 5 hours with 2 g of andydrous ammonium formate. The solid reaction mass was boiled with 10 ml of 20% alcoholic potassium hydroxide and then distilled with steam, the distillate being acidulated with hydrochloric acid and evaporated to dryness. The resultant crystals of the dihydrochloride had a m.p. of 205-207° after recrystallization from absolute alcohol. Yield: 0.35 g (25% of the theoretical).

5.25 mg substance: 0.388 ml N_2 (19°, 745 mm). Found %: N 8.35.
$C_{16}H_{20}ON_2 \cdot 2HCl$. Computed %: N 8.51.

γ-Keto-γ-phenyl-α-(2-nitrophenyl)-propylene (XVII). This was synthesized from a mixture of 3 g of o-nitrobenzaldehyde in 12 ml of absolute alcohol and 2.9 g of acetophenone in 13 ml of absolute alcohol with sodium methylate (0.32 g of sodium and 3.2 g of absolute methanol), by the method used for synthesizing the ketone (XXIII). Recrystallization from alcohol yielded light yellow crystals with a m.p. of 119-120°, which are freely soluble in benzene and alcohol, but are insoluble in water and ether. Yield: 2.2 g (44% of the theoretical).

5.86 mg substance: 0.295 ml N_2 (22°, 754 mm). Found %: N 5.63.
$C_{15}H_{11}O_3N$. Computed %: N 5.53.

γ-Keto-γ-phenyl-α-(2-aminophenyl)-propylene (XVIII). This was synthesized by reducing a boiling solution of 2 g of the nitro ketone (XVII) in 45 ml of absolute benzene by gradually adding, with constant stirring, 20 g of activated cast-iron filings (previously processed with 5 ml of concentrated hydrochloric acid and dried in a vacuum desiccator). After the filings had been added, the reaction mixture was stirred for half an hour, 1 ml of water was added, and another 7 ml of water was added in the course of 7 hours of boiling and stirring. The cast-iron filings were filtered out and washed twice with hot benzene. A stream of hydrogen chloride was passed through the chilled combined benzene extracts until saturation was complete, and the precipitated hydrochloride of the amine was filtered out and washed with absolute benzene. Light-yellow needles with a m.p. of 109-110°, soluble in alcohol or hot water, and insoluble in ether or benzene. After the hydrochloride was filtered out of the benzene, the solvent was evaporated, yielding 0.9 g of the unreacted nitro ketone, with a m.p. of 119-120°. The yield of the hydrochloride of γ-keto-γ-phenyl-α-(2-aminophenyl)-propylene was 0.9 g (80% of the theoretical, based on the nitro ketone entering the reaction).

5.83 mg substance: 0.29 ml N_2 (21°, 745 mm). Found %: N 5.55.
$C_{15}H_{14}ONCl$. Computed %: N 5.40.

Treating an aqueous solution of the hydrochloride with potash and then extracting repeatedly with ether yielded light-yellow crystals of the amine base. M.p. 96-97° after recrystallization from 70% alcohol. Yield: 0.65 g (85% of the theoretical).

4.635 mg substance: 0.26 ml N_2 (18°, 741 mm). Found %: N 6.31.
$C_{15}H_{13}ON$. Computed %: N 6.28.

γ-Keto-γ-(2-nitrophenyl)-α-phenylpropylene (XIX). Like the ketone (XXIII), this was synthesized from a mixture of 1.03 g of benzaldehyde dissolved in 5 ml of absolute alcohol, 1.6 g of o-nitroacetophenone dissolved in 5 ml of absolute alcohol, and a sodium methylate solution (0.19 g of sodium in 2 g of absolute methanol) as colorless crystals with a m.p. of 123-124° after recrystallization from alcohol. Readily soluble in alcohol or benzene, sparingly soluble in ether, and insoluble in water. Yield: 1.8 g (73.5% of the theoretical).

3 mg substance: 0.155 ml N_2 (21°, 734 mm). Found %: N 5.68.
$C_{15}H_{11}O_3N$. Computed %: N 5.53.

o-Nitroacetophenone was prepared by condensing the acid chloride of o-nitrobenzoic acid with sodium acetoacetate.

γ-Keto-γ-(2-aminophenyl)-α-phenylpropylene (XX). This was synthesized as the hydrochloride by reducing 3 g of the nitro ketone (XIX) in 65 ml of absolute benzene with 30 g of activated cast-iron filings as has been described above for γ-keto-γ-phenyl-α-(2-aminophenyl)-propylene. Dark red crystals with a m.p. of 182-183°, soluble in alcohol and in hot water, insoluble in ether or benzene. The yield was 1.3 g (70%, based on the nitro ketone entering the reaction). (1.2 g of the original ketone was recovered).

4.1 mg substance: 0.21 ml N_2 (21°, 734 mm). Found %: N 5.63.
$C_{15}H_{14}ONCl$. Computed %: N 5.40.

γ-Keto-γ-(2-nitrophenyl)-α-(4-methoxyphenyl)propylene (XXI). This was synthesized by the method described above, using 1.6 g of 4-methoxybenzaldehyde dissolved in 5 ml of absolute alcohol, 1.9 g of *o*-nitroacetophenone, in a solution of sodium methylate (0.19 g of sodium in 2 ml of methanol); the yield was 1.6 g (50% of the theoretical) of light-yellow crystals, sparingly soluble in ether and freely soluble in hot alcohol. M.p. 98-99° after recrystallization from alcohol.

3.56 mg substance: 0.165 ml N_2 (20°, 744 mm). Found %: N 5.19.
$C_{16}H_{13}O_4N$. Computed %: N 4.94.

γ-Keto-γ-(2-aminophenyl)-α-(4-methoxyphenyl)-propylene (XXII). The reduction of 1.6 g of the nitro ketone (XXI) with 2.5 g of metallic tin, 13 g of 20% hydrochloric acid being added gradually and the whole being heated to 70-80° for 3 hours with constant stirring, yielded a thick viscous mass that solidified upon cooling. The reaction product was recovered from the acid solution, dissolved by heating in alcohol, filtered, and treated with ether after it had cooled. The precipitated yellow crystals of the hydrochloride of γ-keto-γ-(2-aminophenyl)-α-(4-methoxyphenyl)-propylene was freely soluble in alcohol or hot water, but insoluble in ether or benzene. The melting point was 222-224° after refining from a mixture of alcohol and benzene. Yield: 0.5 g (30% of the theoretical).

4.09 mg substance: 0.17 ml N_2 (22°, 752 mm). Found %: N 4.64.
$C_{16}H_{16}O_2NCl$. Computed %: N 4.83.

SUMMARY

A description is given of the synthesis of compounds that contain the proved or hypothetical elements of the structure of the alkaloid colchicine. The following compounds have been synthesized:

I. Derivatives of α,β-diphenylethylamine: α-(4-hydroxyphenyl)-β-phenylethylamine; α-(4-methoxyphenyl)-β-phenylethylamine; α-(2,5-dimethoxyphenyl)-β-phenylethylamine; and α,β-di-(4-methoxyphenyl)-ethylamine.

II. Derivatives of α,γ-diphenylpropylamine: α-(phenyl)-γ-(2-chlorophenyl)-propylamine and α-(phenyl)-γ-(4-methoxyphenyl)-γ-(amino)-propylamine.

III. Derivatives of β,δ-(diphenyl)-butylamine: β,δ-di-(4-methoxyphenyl)-butylamine and β-(4-methoxyphenyl)-δ-(phenyl)-butylamine.

IV. Derivatives of γ-keto-α,γ-diphenylpropylene: γ-keto-γ-phenyl-α-(4-methoxyphenyl)-propylene; γ-keto-γ-phenyl-α-(2-nitrophenyl)-propylene; γ-keto-γ-phenyl-α-(2-aminophenyl)-propylene; γ-keto-γ-(2-nitrophenyl-α-(phenyl)-propylene; γ-keto-γ-(4-aminophenyl)-α-(phenyl)-propylene; γ-keto-γ-(2-nitrophenyl)-α-(4-methoxyphenyl)-propylene; and γ-keto-γ-(2-aminophenyl)-α (4-methoxyphenyl)-propylene;

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